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THE UNIVERSITY OF ALBERTA

THE SOLVOLYSIS AND REARRANGEMENT OF

α-ARYLETHYL 2,6-DIMETHYLBENZENESULFINATES

BY

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A THESIS

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled, "The Solvolysis and Rearrangement of ∝-Arylethyl 2,6-Dimethylbenzenesulfinates", submitted by Robin Arthur McLaren, B. Sc., in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

ABSTRACT

α-Phenylethyl and α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzene-
sulfinates have been synthesised. In each case one pure diastereomer was
isolated. Mixtures rich in the other diastereomer have also been obtained.

In ethanol and aqueous ethanol both esters give solvolysis products
and the corresponding sulfone. In ethanol the rates of solvolysis and
rearrangement of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate
are four to five powers of ten faster than those of the unsubstituted
ester. This substituent effect is of the order expected for an ionic
reaction. The sensitivity of both the solvolysis and rearrangement
reactions to changes in solvent and the presence of salts is consistent
with an ionic mechanism.

For both esters no common ion rate depression is observed during
solvolysis and the yield of sulfone is unaffected by the presence of
added 2,6-dimethylbenzenesulfinate ion. Under comparable conditions the
reaction of the corresponding bromides in the presence of 2,6-dimethyl-
benzenesulfinate ion gives rise to negligibly small amounts of sulfone.
These results are consistent with an ionic intramolecular mechanism of
sulfone formation. Ion pair return has thus been detected by the sulfinate-
sulfone rearrangement.

In 60% ethanol optically active α-phenylethyl 2,6-dimethylbenzene-
sulfinate gives sulfone of almost completely retained configuration and
solvolysis products of partially inverted configuration. The polarimetric
rate of reaction is identical within experimental error with the overall
rate of reaction.

In 80% ethanol the solvolysis and rearrangement of α-(p-methoxy-phenyl)ethyl 2,6-dimethylbenzenesulfinate are affected to different extents by the addition of sodium azide. The intermediates involved in the two reactions therefore differ.

In the case of both esters the two diastereomers give about the same fractions of solvolysis and rearrangement but differ in their rate of reaction. The rate of reaction of the diastereomer which was not isolated in the pure state was estimated to be about 1.6 times faster than the other diastereomer for both esters. The diastereomers have been equilibrated in pyridine in the presence of pyridine hydrobromide. The equilibrium mixture in each case contains about 46% of the fast reacting diastereomer.

During the solvolysis of the pure diastereomer of each ester the other diastereomer is formed. This isomerisation reaction shows the same sensitivity to the presence of the methoxy substituent as do the solvolysis and rearrangement reactions and is hence ionic. In the case of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate in ethanol the isomerisation reaction has been shown to be intramolecular. Thus the isomerisation reaction in this case is an example of ion pair return.

TABLE OF CONTENTS

INTRODUCTION

Solvolysis has been defined as a "nucleophilic substitution reaction in which the solvent is the nucleophilic reagent," (52), i.e.,

R.X + SOH ⟶ R.OS + HX,

where SOH = solvent.

Many such reactions have been shown to involve ionisation of the substrate and in such cases the solvolysis product is often found to be partially inverted in configuration (53). Since a free carbonium ion was expected to give racemic solvolysis products, Hammett suggested in 1940 that these results could be interpreted in terms of ion pairs as intermediates in the solvolysis reaction (54). The first direct experimental evidence of the importance of ion pairs in solvolysis reactions was obtained by Young, Winstein and Goering in 1951 (10). They observed a downward drifting rate in the acetolysis of α,α-dimethylallyl chloride, the final value of the rate constant being that observed for γ,γ-dimethylallyl chloride, which was the only chloride isolable after 30 per cent solvolysis. Added chloride ion had no effect on the rate of the reaction and common ion rate depression would be expected if the rearrangement involved combination of chloride ion and free allylic carbonium ion. These workers distinguished "external return" from free ions and "internal return" from ion pairs. Subsequently these phenomena have been redefined as "external ion return" and "ion pair return" respectively (11). Since then much evidence has been accumulated, only the key papers of which will be discussed here.

A theoretical treatment of ion pair phenomena has been presented (11) based on the reaction scheme

$$R - X \rightleftharpoons R^+ X^- \rightleftharpoons R^+ // X^- \rightleftharpoons R^+ + X^-$$

where two different ion pair species are defined. Products may be formed from any or all of the intermediates. $R^+ X^-$ is the "intimate ion pair" consisting of two ions of opposite charge with no solvent molecules between them. $R^+ // X^-$ is the "solvent separated ion pair" where a small number of solvent molecules are interposed between the ions which are held together by electrostatic attraction. The evidence for the existence of two types of ion pairs rests mainly on the non-identity of the solvolytic rate constant and some other rate constant (such as the polarimetric rate constant) and the existence of the "special salt effect" in certain systems.

The acetolysis of threo-3-p-anisyl-2-butyl p-bromobenzene-sulfonate was shown not to involve external ion return (from free ions) (11). The polarimetric rate constants under various conditions were found to be greater than the titrimetric rate constants by a factor of 4 to 5 (12). In this case, since a symmetrical ion is expected from anchimerically assisted ionisation, the polarimetric rate constant is probably equal to the ionisation rate constant. When lithium perchlorate was added to the reaction mixture the polarimetric rate constant showed the usual linear dependence on the concentration of salt (13). However the titrimetric rate showed this dependence only at fairly high salt concentration and extrapolation to zero salt concentration gave a value of k_{ext}^o greater than k_t^o (observed in the absence of salt) by a factor of 2 to 3. At no finite salt concentration is the

titrimetric rate equal to the polarimetric rate. At low salt concentra-
tions (0-0.02M) the effect of salt on the rate of solvolysis is much
greater than that observed at higher concentrations of the salt. These
effects are illustrated in Figure I.

Since this special salt effect was not observed to affect the
polarimetric rate it cannot be an effect on the ionisation step and must
be connected with the dissociation of an ion pair. If no ion pair
return occurred the polarimetric and titrimetric rates would be equal.
Since the two rates are never equal it follows that a portion of ion
pair return cannot be eliminated by the presence of lithium perchlorate.
Hence two intermediates are involved, which must both be ion pairs as
it was shown that free ions are not formed under these conditions (11).
The interpretation suggested was that the presence of lithium perchlor-
ate removes solvent separated ion pairs from the system by formation of
$R^+//ClO_4^-$ which solvolyses rapidly, thus reducing the amount of return
to yield starting material. More recently a detailed analysis of the
mechanism of the special salt effect has been published (14). The esta-
blished mechanism is an exchange reaction between the solvent separated
ion pair and a lithium perchlorate ion pair to give $R^+//ClO_4^-$.

At the time that this work was commenced ion pairs had been
demonstrated to be of importance only in the solvolysis of compounds
which gave rise to bridged ions and certain allylic systems. No evi-
dence of their importance in the reactions of open carbonium ions was
available. Since the carbonium ion in ion pairs of the general type
$R^+ X^-$ is not necessarily racemic it is not possible to equate the polari-
metric rate with the ionisation rate. Ion pair return in the case
of halides, carboxylates and sulfonates, the leaving groups normally
used in the study of solvolytic reactions, might give racemisation,
but not necessarily so. Ion pair return in the case of sulfinate
esters could give racemisation and also an unreactive rearranged
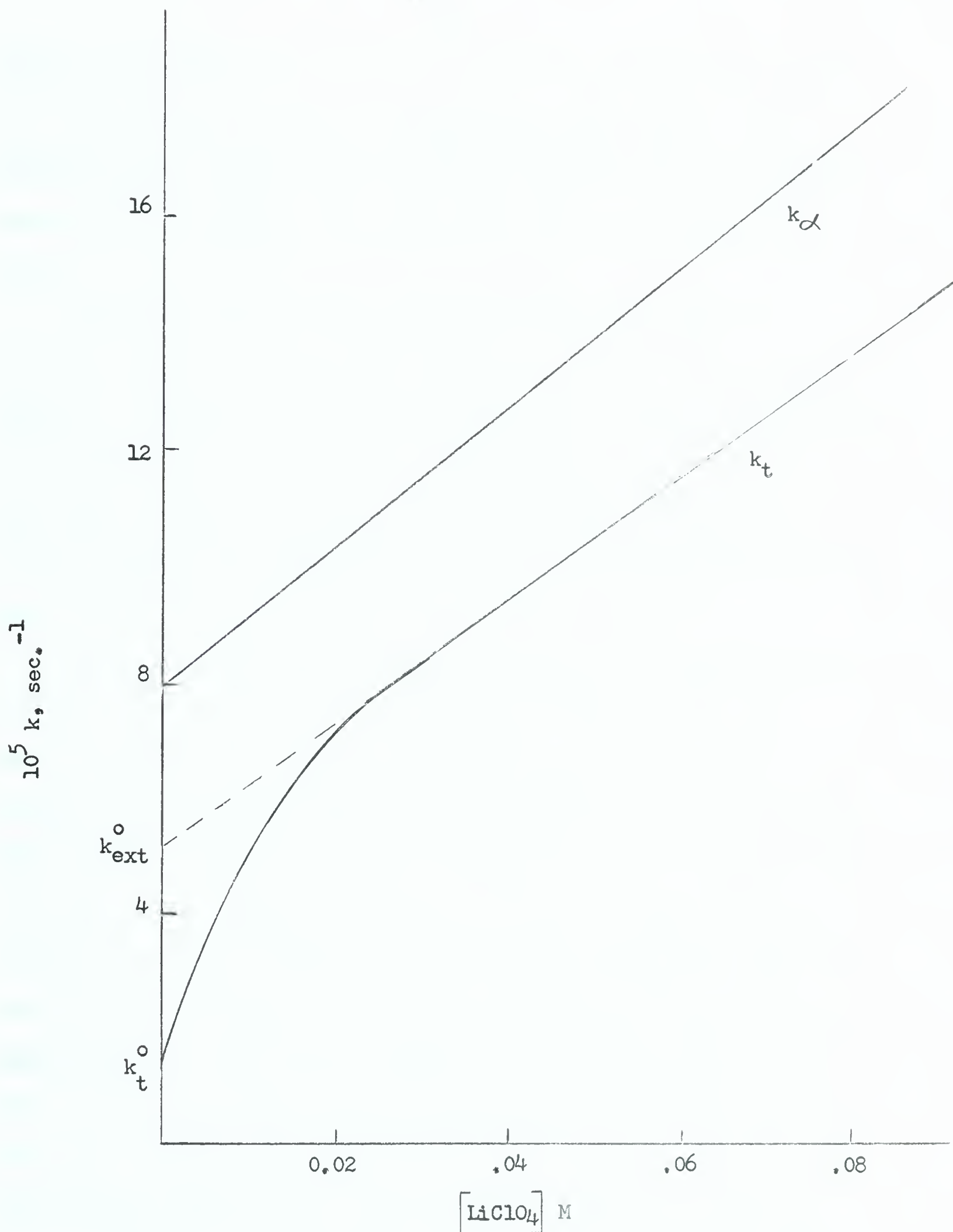
FIGURE I

Effect of lithium perchlorate on acetolysis of threo-3-p-anisyl-2-butyl

p-bromobenzenesulfonate at 25° (taken from S. Winstein & G. C. Robinson,

J. Am. Chem. Soc., 80, 169 (1958))

product, the sulfone. It was therefore decided to examine the solvoly-
sis of such esters with a view to detecting ion pair return. Some
evidence in the literature discussed below indicated that the sulfinate
ester-sulfone rearrangement reaction could in fact occur by ion pair
return.

Although sulfinate esters were first prepared in 1885 (1)
relatively little work has been done on their reactions under controlled
conditions. Since the present work was directed to studying their ionisa-
tion reactions only those systems in which the results are consistent
with carbon-oxygen bond cleavage will be discussed. A discussion of
sulfur-oxygen bond cleavage in these compounds has been presented else-
where (2).

Kenyon, Phillips and co-workers investigated the reactions of a
series of sulfinate esters during the course of their work on the
Walden Inversion. They found that α-phenylethyl p-toluenesulfinate on
standing at room temperature for several days gave, among other products,
α-phenylethyl p-tolyl sulfone which was found to be racemic (3). Also,
solvolysis of this compound in ethanol or acetic acid gave the corres-
ponding ethyl ether or acetate with racemisation or slight inversion of
configuration (4). However, in ethanol containing potassium carbonate,
α-phenylethanol was formed with complete retention of configuration
(3,4). Carbon-oxygen bond cleavage would give rise to α-phenylethyl
ethyl ether and not α-phenylethanol, which is the expected product from
sulfur-oxygen bond cleavage. The formation of sulfone was favored in
solutions where acid catalysis was possible (4). Thus in this system
carbon-oxygen bond cleavage was demonstrated to occur but not necessarily

under neutral conditions.

Similar results were obtained with the p-toluenesulfinate of
ethyl 3-hydroxy-3-phenylpropionate (5). In ethanol the corresponding
ethyl ether was obtained with partial inversion, but in ethanol-
potassium carbonate, acetic acid or formic acid sulfur-oxygen bond
cleavage occurred.

The most extensive study of the reaction by Kenyon's group was
carried out on α-phenylethyl p-toluenesulfinate. The compound was
dissolved in various solvents and allowed to react either at room
temperature or at 80° (6). It was found that sulfone formation was
favored in media of high dielectric constant and that the yield of sulfone
was greatly reduced by the addition of a nucleophilic species (e.g.,
formate ion in formic acid). Kenyon suggested that these results should
be explained on the basis of sulfone formation by an ionic mechanism.
Further evidence was obtained by an examination of the reaction of the
optically active ester in formic acid. In formic acid a 60 per cent
yield of racemic sulfone was isolated after purification, but in formic
acid containing sodium formate the yield of sulfone was reduced to 10
per cent (purified) and it was shown to have been formed with 63 per
cent retention of configuration. Kenyon suggested that racemic sulfone
was formed by an ionic mechanism and retained sulfone by a non-ionic
rearrangement. An alternative explanation is that retained sulfone is
formed by ion pair return. The fact that the α-phenylethyl formate
isolated from the reaction in formic acid-sodium formate is also
partially retained in configuration indicates that carbon-oxygen bond
cleavage is not the exclusive mechanism of solvolysis under these

conditions.

Cope and co-workers examined the reaction of γ-methylallyl
benzenesulfinate and α-methylallyl benzenesulfinate in toluene at 100°
and in each case isolated a low yield of γ-methylallyl phenyl sulfone
(7). They suggest that this result can be interpreted as occurring by
an allylic rearrangement to give sulfone followed by formation of an
equilibrium mixture of the two possible sulfones, by an allylic rearrange-
ment to give a mixture of two sulfinates followed by another rearrange-
ment to give sulfone or by an ionic mechanism.

Wragg, McFadyen and Stevens studied the rearrangements of a
number of sulfinates (8). They found that benzhydryl p-toluenesulfinate
rearranged to the corresponding sulfone in acetic acid and nitromethane
but not in acetonitrile, benzene or toluene. In the last three solvents
the reaction did occur in the presence of p-toluenesulfinic acid. In
acetic acid in the presence of p-chlorobenzenesulfinic acid some
benzhydryl p-chlorophenyl sulfone could be isolated. The rates of re-
arrangement of the homogeneous p-toluenesulfinates were found to be in
the following order: o-methylbenzhydryl $>$ benzhydryl $>$ α-phenylethyl.
Benzhydryl p-chlorobenzenesulfinate was also found to react faster than
benzhydryl p-toluenesulfinate. These relative rates are in the order
expected for a rate determining ionisation, which may however involve
acid catalysis as no base was added and no actual rate constants were
measured. The other results are consistent with ionisation, especially
the fact that exchange was shown to occur.

Bunton and Hendry examined the solvolysis of benzhydryl
p-toluenesulfinate in 60 per cent dioxane-water (9) and obtained evidence

that the acid catalysed reaction gave a substantial amount of carbon-oxygen bond cleavage, the actual amount depending on the acid catalyst used. The hydrolysis under initially neutral conditions was found to show autocatalytic behavior.

Much of the work discussed above indicates that the sulfinate ester-sulfone rearrangement is an ionic reaction and the formation of of sulfone of retained configuration from optically active α-phenyl-ethyl p-toluenesulfinate (6) is indicative of ion pair return. It was therefore reasonable to believe that ion pair return could be detected in open chain carbonium ion systems, if it occurred, by the use of a sulfinate ion leaving group. It was decided to study α-arylethyl esters as they contain an asymmetric centre and the stereochemistry of the reaction could be determined by the use of optically active esters. Since this work was commenced other types of evidence for ion pair return in open chain carbonium ion systems have been published.

In the solvolysis of optically active p-chlorobenzhydryl chloride in 80 per cent acetone at 25° the racemisation rate was greater than the titrimetric rate by a factor of 2.5 (56). The racemisation rate was greater than the sum of the titrimetric and exchange (with radioactive chloride ion) rates by a factor of two. Since the exchange reaction is a measure of possible common ion rate depression it follows that the racemisation occurs without the formation of free ions and hence must involve ion pair return. Similar results were obtained in acetic acid (60) and in acetone (61). Almost exactly the same results were apparently obtained by Pocker (57) on the solvolysis of optically active $C_6H_5 \cdot CDCl \cdot C_6D_5$ and $C_6H_5 \cdot CHCl \cdot C_6D_5$ in 80 per cent acetone at 25°.

Goering and co-workers have presented evidence for the existence

of two types of ion pairs. These workers found that the solvolysis of

optically active carbonyl-^{18}O-p-chlorobenzhydryl p-nitrobenzoate in 80

and 90 per cent aqueous dioxane was accompanied by racemisation and

randomisation of the carboxyl oxygen atoms in the ester (15). Both these

reactions were shown to be at least 99 per cent intramolecular. In the

presence of 0.14M sodium azide randomisation still occurred but racemi-

sation was completely eliminated (16). This clearly shows that two

different ion pair intermediates are involved, return from one giving

rise to both racemisation and randomisation and from the other to

randomisation only.

Ion pair return has also been detected in the reaction of trityl

2-methylbenzenesulfinate in acetonitrile at room temperature (55). The

ester rearranges to trityl 2-methylphenyl sulfone. The addition of

tetrabutylammonium azide diverts a portion of the reaction to trityl

azide but has little effect on the rate of disappearance of ester.

About 55 per cent of the rearrangement reaction is not diverted by azide

ion. The results were interpreted in terms of two intermediates, an

intimate ion pair and either a solvent separated ion pair or free ions, or both.

Ion pair return has also been detected in two cases by the use of

a rearranging leaving group in a similar manner to the proposed detec-

tion of such return by the sulfinate ester-sulfone rearrangement.

In the ethanolysis of benzhydryl thionbenzoate intramolecular

rearrangement to the thiolbenzoate occurs by ion pair return during the

solvolysis (17). In solvents up to the polarity of acetonitrile

benzhydryl thiocyanate rearranges to benzhydryl isothiocyanate mainly by

ion pair return (58).

CHAPTER I

THE IONISATION OF ARENESULFINATE ESTERS

RESULTS

α-Phenylethyl o-nitrobenzenesulfinate

The route illustrated in Figure II was used for the preparation of o-nitrobenzenesulfinic acid. The reaction between o-nitrochloro-benzene and sodium disulfide (19,20) yielded di-(o-nitrophenyl) disulfide. Oxidation of this compound with nitric acid-hydrochloric acid in the presence of chlorine (21,22) gave o-nitrobenzenesulfonyl chloride which could be reduced either with hydrazine (23) or with stannous chloride-hydrochloric acid in ethanol (24) to o-nitrobenzene-sulfinic acid.

Sulfinic acids are reported to show infrared absorption near 1090 $cm.^{-1}$ (48) and in the above compound a strong band is observed at 1075 $cm.^{-1}$ (nujol). Titration with sodium methoxide indicated a molecular weight of 198 (calculated 187) corresponding to a purity of 94.4 per cent. Sulfinic acids are known to be converted to a corresponding sulfonyl chloride by reaction with chlorine (25). Reaction of o-nitrobenzenesulfinic acid with chlorine gave o-nitrobenzenesulfonyl chloride identical with that obtained above.

The acid was allowed to react first with thionyl chloride and then with α-phenylethanol in pyridine to give α-phenylethyl o-nitro-benzenesulfinate. The infrared spectrum showed bands at 1120 and 865 $cm.^{-1}$.

FIGURE II

The preparation of o-nitrobenzenesulfinic acid
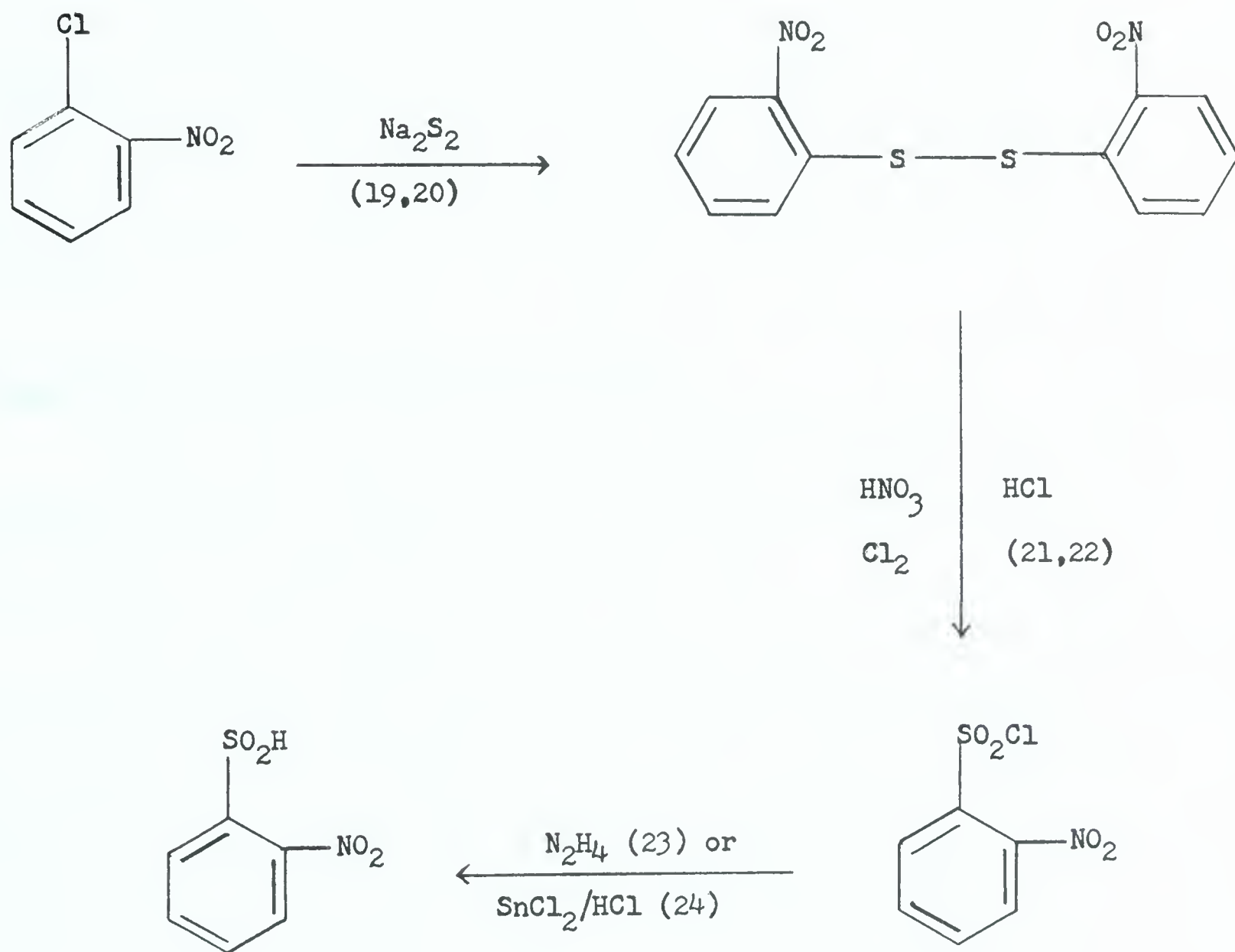
A band in the first region has been assigned to sulfinate esters (48) and a broad band in the second region has been observed in the spectrum of a number of sulfinate esters in this laboratory. A specific assignment of this band to a particular vibrational mode of the sulfinate ester grouping has not however been made.

A solution of α-phenylethyl o-nitrobenzenesulfinate in dry ethanol containing sodium acetate showed complete reaction at reflux temperature in less than six hours. A crystalline product could be isolated in 37 per cent yield and on the basis of its infrared spectrum (880 and 1140 $cm.^{-1}$ in CS_2) it was formulated as ethyl o-nitrobenzene-sulfinate.

Preparation of 2,6-dimethylbenzenesulfinates

Attention was then shifted to 2,6-dimethylbenzenesulfinates. The compounds studied were α-phenylethyl 2,6-dimethylbenzenesulfinate and the corresponding α-(p-methoxyphenyl)ethyl ester.

Reduction of acetophenone with lithium aluminum hydride in ether gave α-phenylethanol and similarly reduction of p-methoxyacetophenone gave α-(p-methoxyphenyl)ethanol. This latter compound was in the early part of this work prepared from anisaldehyde and methyl magnesium iodide. It was found that it was necessary to cool the reaction mixture in an ice bath and that the alcohol had to be separated from an impurity by chromatography on alumina. The impurity was identified as di-(α-p-methoxyphenylethyl) ether.

Treatment of 2,6-dimethylaniline with nitrous acid followed by saturation of the solution with sulfur dioxide and the addition of

copper powder gave 2,6-dimethylbenzenesulfinic acid (26). Its structure

follows from its method of preparation, its infrared spectrum (1050 cm^{-1}

in nujol) and its equivalent weight of 170 (calculated 170). For

kinetic work it was recrystallised from wet ethanol, but was used for

preparative work without recrystallisation.

Treatment of the acid with thionyl chloride in pentane gave

2,6-dimethylbenzenesulfinyl chloride which was used immediately after

removal of excess thionyl chloride to prepare the esters. The compound

is very susceptible to hydrolysis. The general method of preparation of

the esters was to dissolve the acid chloride in anhydrous pyridine,

cool the solution in dry ice-acetone and add the appropriate alcohol.

The mixture was allowed to warm up to 0° and poured on to ice-hydro-

chloric acid. The crude ester was isolated by ether extraction.

Both esters contain two asymmetric centres (the sulfur atom

and the methine carbon atom) and hence can exist in two diastereomeric

forms. In each case both diastereomers were formed in the preparation

and one pure diastereomer could be isolated by recrystallisation.

The nuclear magnetic resonance spectrum of the crude product

from the preparation of α-phenylethyl 2,6-dimethylbenzenesulfinate

contained two peaks of approximately equal intensity at 7.5T and 7.6T.

When the reaction mixture was left for 8 days before work-up the two

peaks were present in the ratio 40:60. Recrystallisation from ether-

pentane yielded one pure diastereomer, m.p. 65.5-67.5°, showing absorp-

tion at 1135 and 880 cm^{-1}. The nuclear magnetic resonance spectrum

showed a singlet at 2.80T, a multiplet at 3.1T, a quartet at 4.79T,

a singlet at 7.59T and a doublet at 8.46T. The relative areas were 8

(for the first two peaks) : 1 : 6 : 3 as would be expected for

⍺-phenylethyl 2,6-dimethylbenzenesulfinate. The assignment of the

peaks in the n.m.r. spectrum of the ester is illustrated below. The

actual spectrum is reproduced in Figure III.
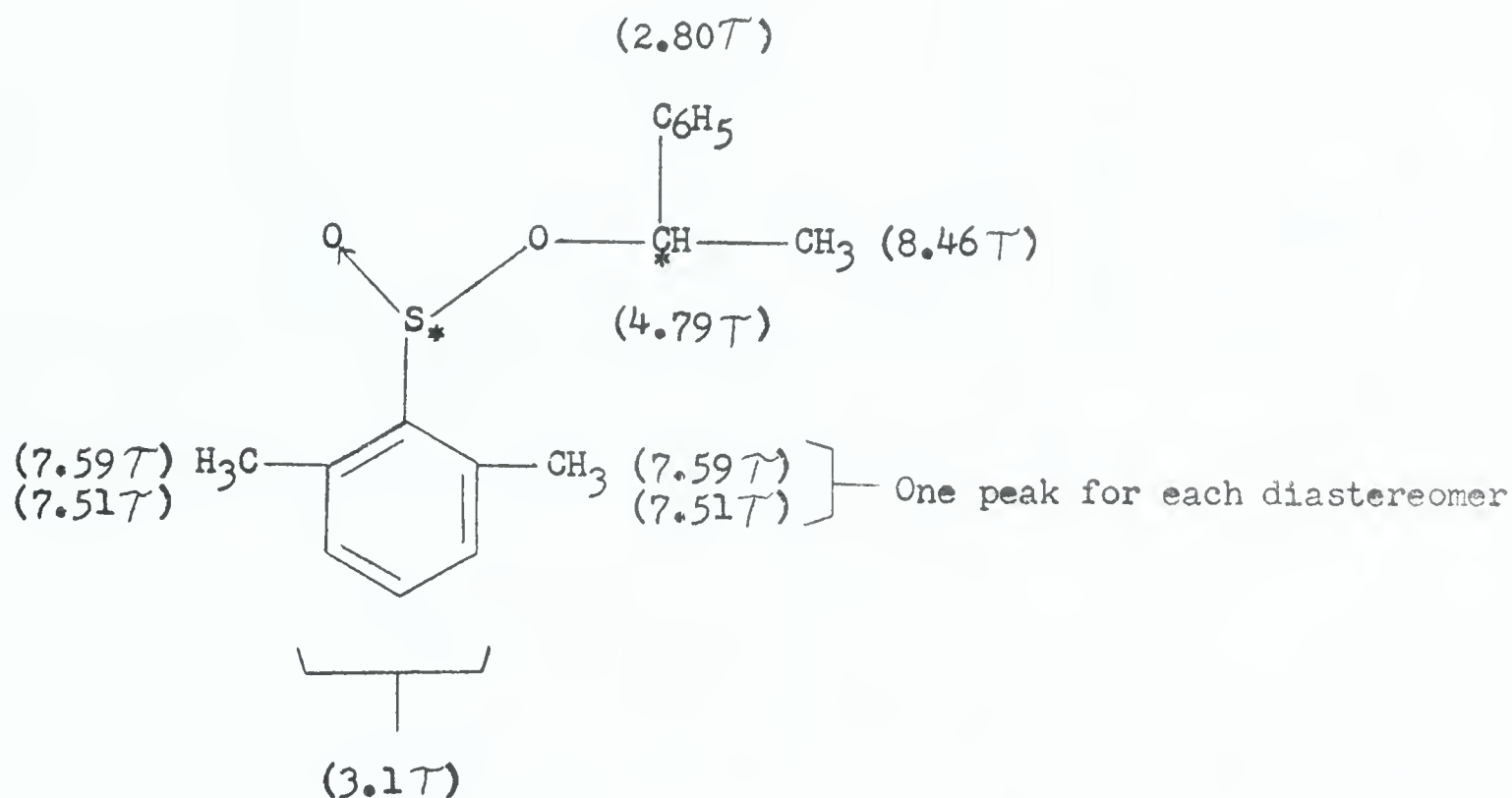
From the mother liquors further samples of ester could be

isolated. Their infrared spectra were superimposable on that of the

pure diastereomer and the nuclear magnetic resonance spectrum differed

only in the region ascribed to the aromatic methyl groups. Two peaks

were present at $7.51\mathcal{T}$ and $7.59\mathcal{T}$ in the ratio 2:1. Recrystallisation

did not significantly affect the composition of these mixtures. The

peak at $7.51\mathcal{T}$ is assigned to the diastereomeric ⍺-phenylethyl 2,6-di-

methylbenzenesulfinate. The equilibration of the two diastereomers

in pyridine and the kinetics and products of solvolysis of the
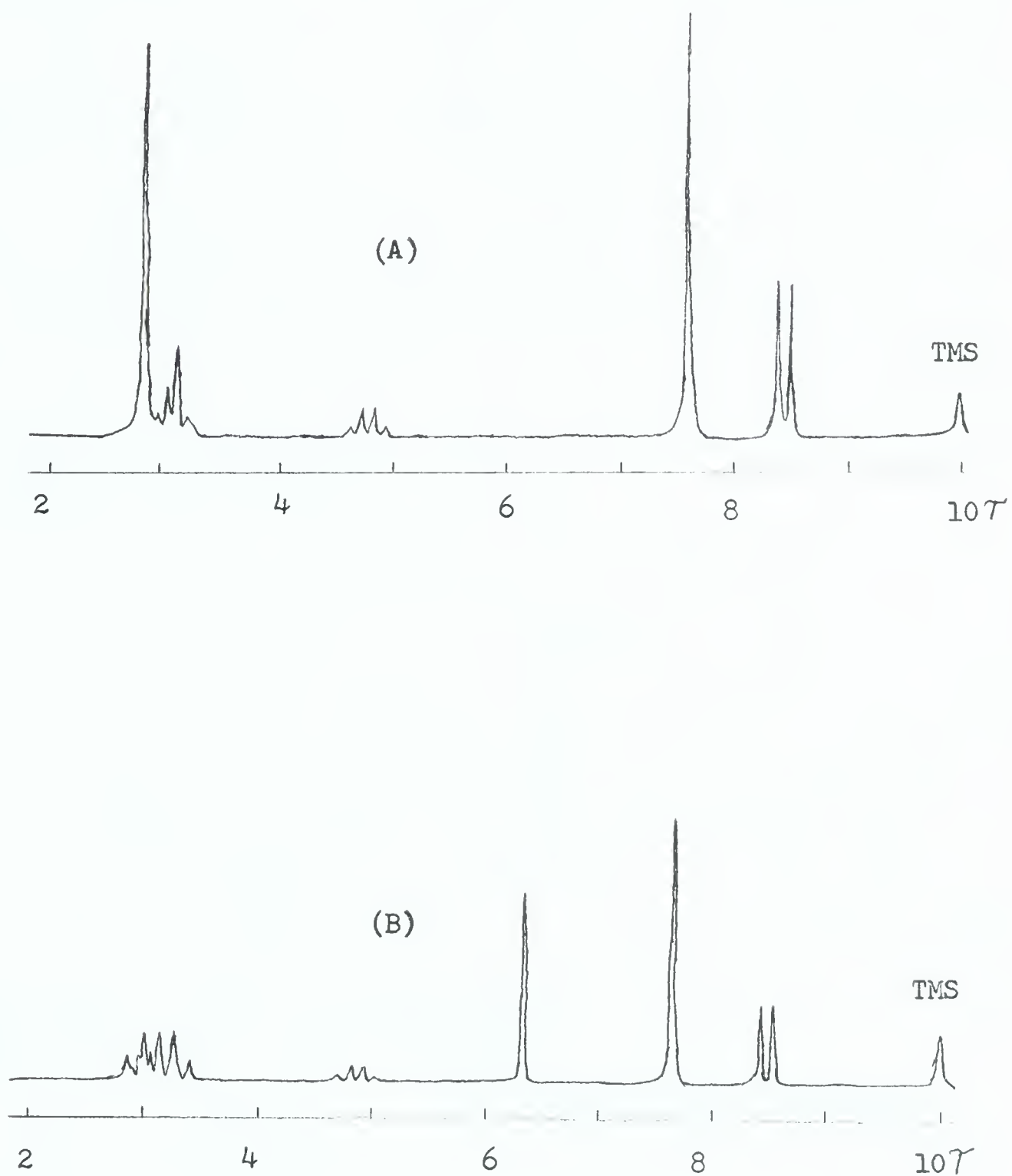
FIGURE III

Nuclear magnetic resonance spectra of diastereomerically pure α-phenyl-ethyl 2,6-dimethylbenzenesulfinate (A) and α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate (B) in CS_2.

diastereomers reported below give further confirmation of this
assignment.

Similarly, the crude reaction product from the reaction of
2,6-dimethylbenzenesulfinyl chloride and α-(p-methoxyphenyl)ethanol
showed two peaks of approximately equal intensity at 7.55τ and 7.64τ.
Recrystallisation from ether or ether-pentane gave one pure diastereomer,
m.p. 69-71°, showing absorption at 1130 and 865 cm.$^{-1}$. The nuclear
magnetic resonance spectrum showed a multiplet at 3.1τ, a quartet at
4.86τ, singlets at 6.39 and 7.64τ and a doublet at 8.49τ. The rela-
tive areas were 7 : 1 : 3 : 6 : 3 as would be expected for α-(p-methoxy-
phenyl)ethyl 2,6-dimethylbenzenesulfinate. The n.m.r. peak assignment is
shown below and the spectrum in Figure III.

One peak for each diastereomer
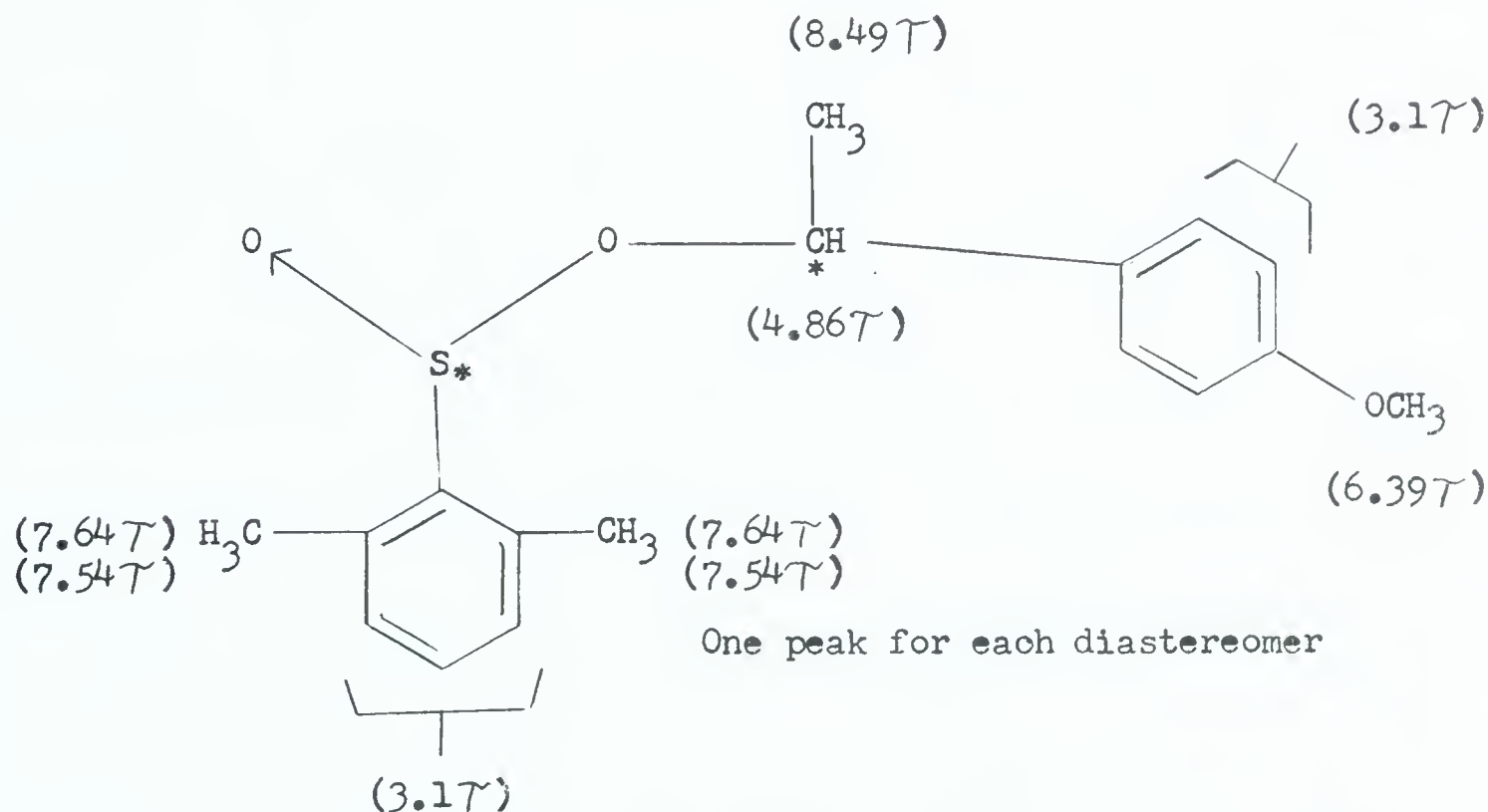
In this case no crystallisation from the mother liquors could
be effected, but the infrared spectrum was superimposable on that of the

pure ester except for a weak band at 1330 cm^{-1} (thiolsulfonate). The

nuclear magnetic resonance spectrum showed a number of minor impurities

to be present, one of which was identified as 2,6-dimethylphenyl

2,6-dimethylbenzenethiolsulfonate (bands at 7.75 and 7.93Υ). The major

peaks were identical with those observed for the pure ester with the

exception that two aromatic methyl peaks due to ester, were observed.

The ratio of these peaks at 7.54 and 7.63Υ was 80 : 20. As above

the peak at 7.54Υ was assigned to the diastereomeric sulfinate ester

and this assignment is supported by equilibration and solvolysis

experiments to be reported below.

Equilibration of Diastereomers

For both esters equilibration of the diastereomers was carried

out. It was found that the nuclear magnetic resonance spectrum of

diastereomerically pure α-phenylethyl 2,6-dimethylbenzenesulfinate was

unchanged when a pyridine solution was allowed to stand at room tempera-

ture but did change on heating in the presence of tetrabutylammonium

bromide. It was also changed in the presence of pyridine hydrobromide

at room temperature. The reaction observed was an equilibration of the

two diastereomers which was however accompanied by decomposition of the

ester. The results are shown in Table I. The percentage of fast

diastereomer (the diastereomer showing the Ar.CH_3 peak at lower field)

was calculated from the relative areas of the peaks at 7.35 and 7.45Υ.

The positions of the peaks are shifted by the change in solvent from

CS_2 to pyridine.

In Run 2-249 decomposition gave the thiolsulfonate together with

another product which was possibly 2,6-dimethylbenzenesulfinic acid.

After 14.9 hours the extent of decomposition was estimated from the

relative areas of the peaks at 7.56 and 7.82 $\mathcal{T}$ (due to thiolsulfonate)

and at 7.35 and 7.45 $\mathcal{T}$ (due to ester) as 38 per cent. In Runs 2-251 and

2-252 the only apparent decomposition product was 2,6-dimethyl-

benzenesulfinic acid. After 91.5 hours in Run 2-251 the extent of

sulfinic acid formation was estimated as 10 per cent from the relative

areas of the peak at 6.9 $\mathcal{T}$ and the ester peaks. Authentic 2,6-dimethyl-

benzenesulfinic acid was added to the solution at this time and the

spectrum taken after a further 33.5 hours. A much more intense peak

was present at 6.9 $\mathcal{T}$. Thiolsulfonate and an unidentified minor product

were also formed under these conditions. The presence of α-phenylethanol

or styrene, which are possible decomposition products, would not be

apparent at low concentration.

The composition of the ester mixture is seen to approach 46 per

cent of the fast diastereomer and 54 per cent of the slow diastereomer

no matter which diastereomer is initially present in excess. The

values of k_{eq} were calculated from the expression

$$k_{eq}t = 2.303 \log (C_{\infty} - C_0)/(C_{\infty} - C),$$

where C represents the percentage of the fast diastereomer in the mixture.

The value of k_{eq} is identical within experimental error no matter which

side the equilibrium is approached from. The spectra of the starting

ester in Runs 2-251 and 2-252 and of the product mixture in Run 2-252

are shown in Figure IV.

A similar series of experiments were carried out using solutions

of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate in pyridine-

100% slow diastereomer

TMS

Equilibrium mixture

TMS

65% fast diastereomer

TMS
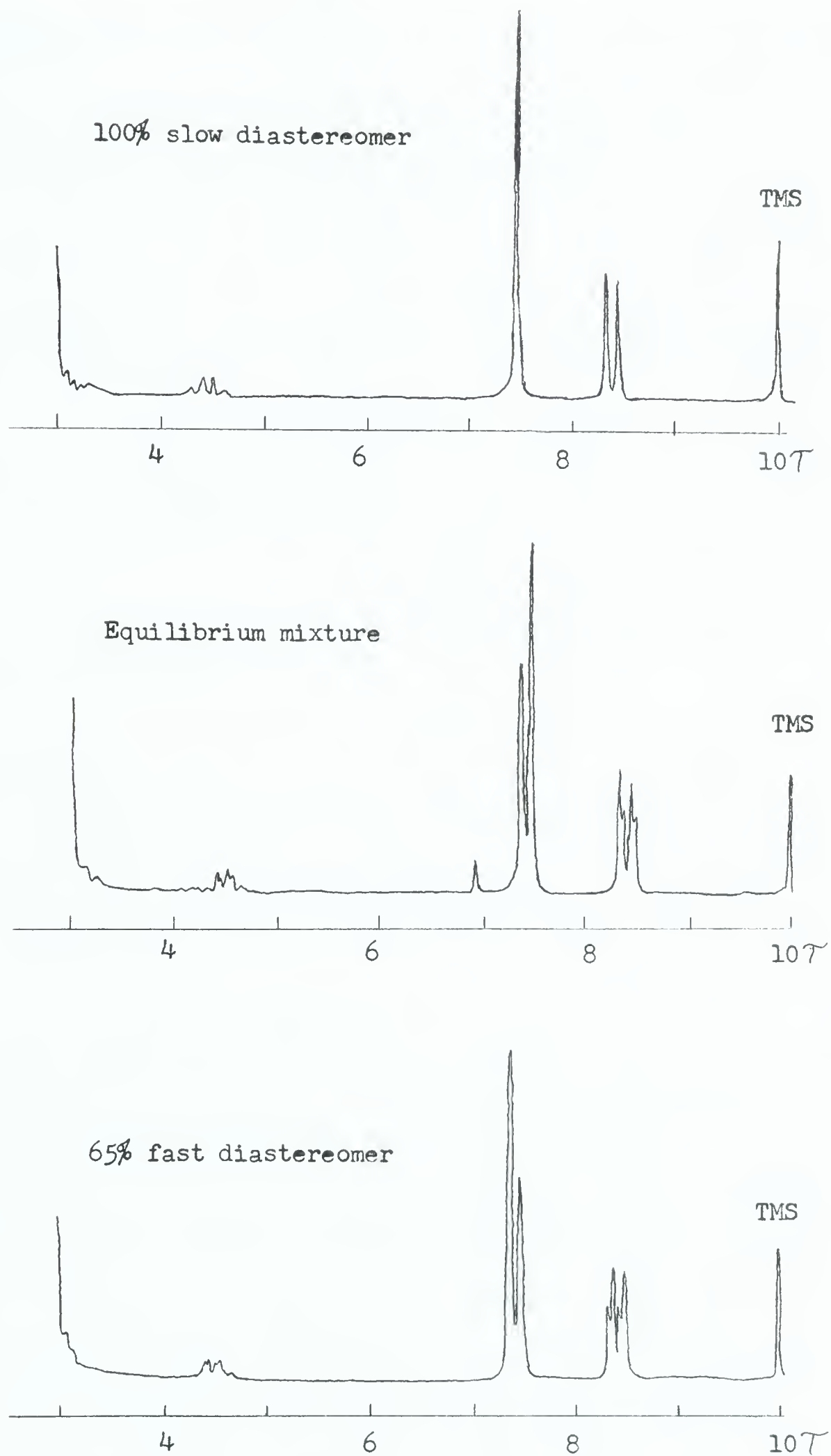
FIGURE IV

Nuclear magnetic resonance spectra of α-phenylethyl 2,6-dimethyl-benzenesulfinate in pyridine.

pyridine hydrobromide at room temperature. The results are reported in Table II. The percentage of fast diastereomer (the diastereomer showing the Ar.CH$_3$ peak at lower field) was calculated from the relative areas of the peaks at 7.33 and 7.42Υ. From the area of the peak at 6.9Υ relative to the ester peaks the maximum amount of decomposition to give 2,6-dimethylbenzenesulfinic acid observed in these runs was estimated as 15-20 per cent. As in the case of the unsubstituted ester, it is seen that the equilibrium mixture and the rate of equilibration are the same when the equilibrium is approached from both sides. The equilibrium mixture contains ca. 46 per cent of the fast diastereomer. The spectra of the starting ester in both runs and of the product mixture in Run 2-257 are shown in Figure V.

Synthesis of Sulfones

The rearrangement product of the α-phenylethyl ester, α-phenylethyl 2,6-dimethylphenyl sulfone, was synthesised by the route shown in Figure VI. Treatment of 2,6-dimethylaniline with nitrous acid, followed by potassium ethyl xanthate gave 2,6-dimethylphenyl ethyl xanthate which was hydrolysed with potassium hydroxide without purification to yield 2,6-dimethylthiophenol. The infrared spectrum of the thiophenol was superimposable on that of an authentic sample. Treatment of α-phenylethanol with thionyl chloride gave α-phenylethyl chloride which was allowed to react with 2,6-dimethylthiophenol and sodium hydroxide in ethanol at reflux temperature. The product, α-phenylethyl 2,6-dimethylphenyl sulfide, was a viscous yellow oil containing some minor impurities (from the n.m.r. spectrum). No attempt was made to

TABLE I

Equilibration of the diastereomeric α-phenylethyl

2,6-dimethylbenzenesulfinates in pyridine

Run (a)	Temp ^oC	Catalyst	[Catalyst]	Time (hrs)	%FD(b)	k_{eq} x 10^5 sec.$^{-1}$
2-249	70.00	Bu$_4$NBr	0.3M	0	0	--
				5.6	45	--
				14.9	47	--
2-251	25	C$_5$H$_5$N.HBr	0.08M	0	0	--
				2.2	trace	--
				19.0	34	2.0
				91.5	44	1.0
				125.0	45	--
2-252	25	C$_5$H$_5$N.HBr	0.05M	0	65	--
				21.3	49	2.4
				51.5	47	--

(a) In this and all subsequent tables the run number is a laboratory notebook reference, e.g., 2-249 refers to page 249 of the second laboratory notebook.

(b) Fast diastereomer.

TABLE II

Equilibration of the diastereomeric α-(p-methoxyphenyl)ethyl

2,6-dimethylbenzenesulfinates in pyridine at 25°

Run	[C$_5$H$_5$N.HBr]	Time (hrs)	%FD	k_{eq} X 10^5, sec.$^{-1}$
2-257	0.05M	0	0	--
		20.9	30	1.4
		43.5	40	1.3
		74.9	44	--
2-258	0.04M	0	80	--
		21.4	56	1.6
		43.8	49	1.5
		75.3	47	--
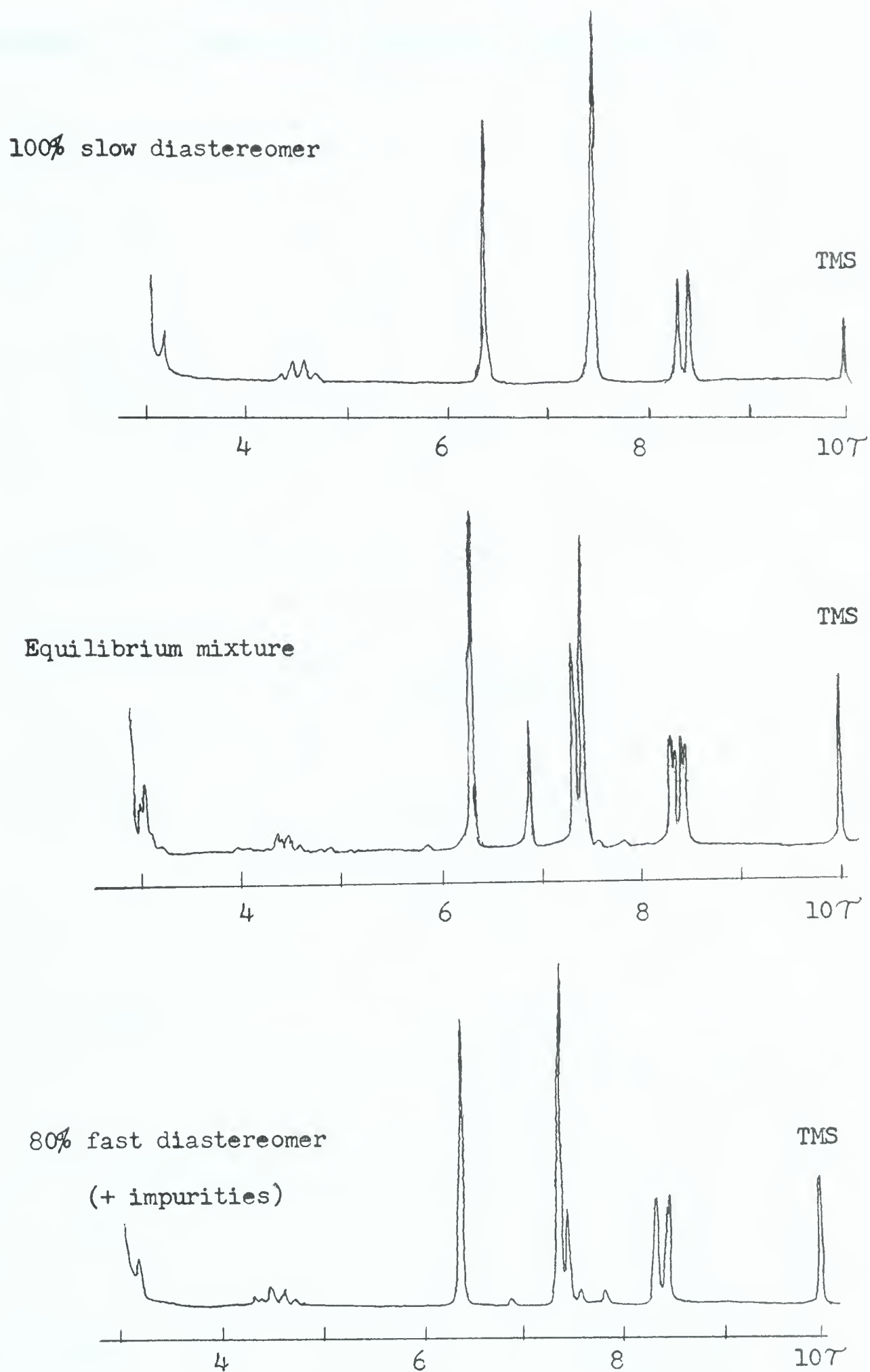
FIGURE V

Nuclear magnetic resonance spectra of α-(p-methoxyphenyl)ethyl

2,6-dimethylbenzenesulfinate in pyridine.

FIGURE VI

The preparation of ⍺-phenylethyl 2,6-dimethylphenyl sulfone
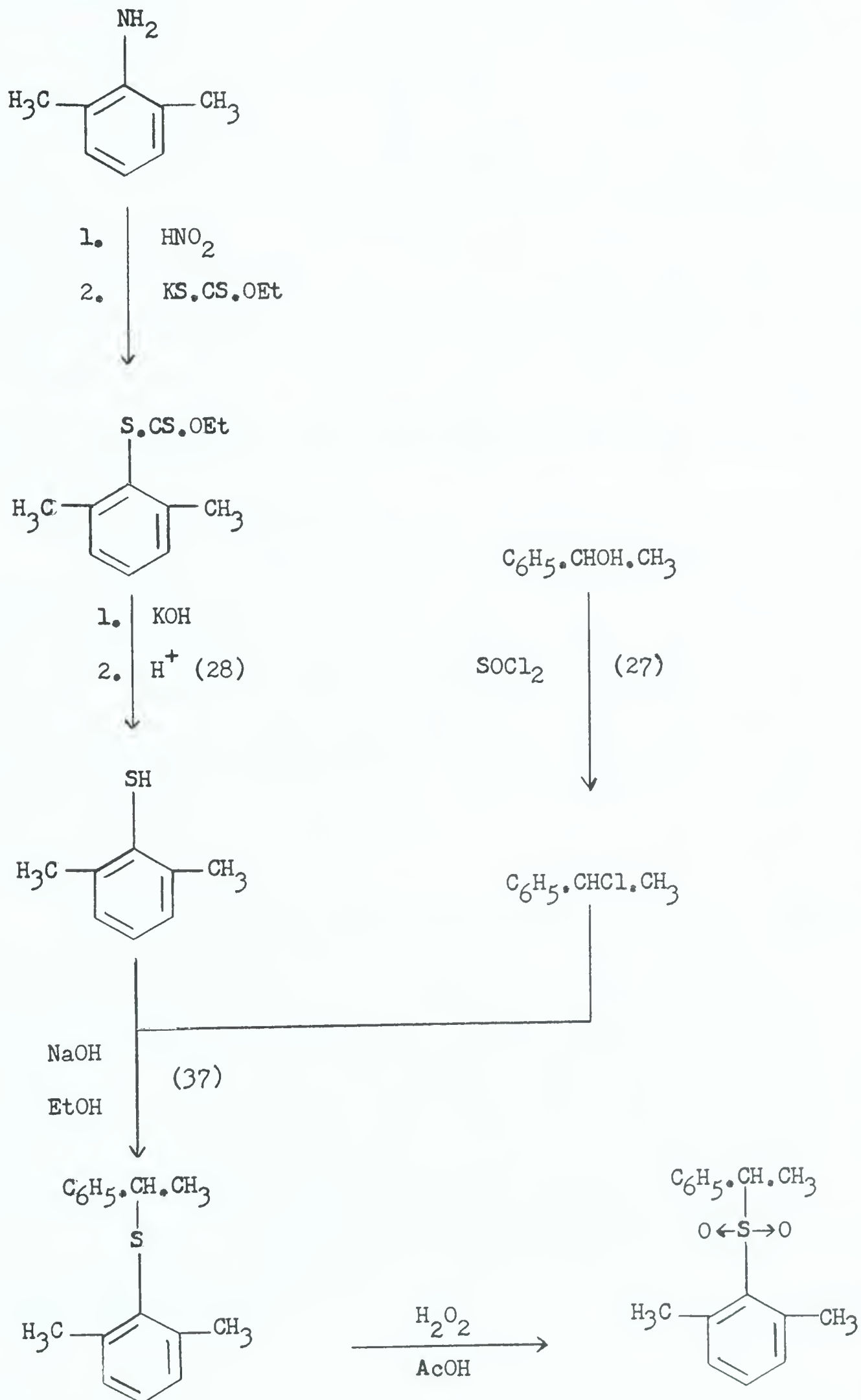
purify the compound as the desired oxidation product, α-phenylethyl

2,6-dimethylphenyl sulfone, is a readily crystallisable compound.

Treatment of the sulfide with chromium trioxide in acetic acid,

at room temperature or on the steam bath, did not give the desired

sulfone. A crystalline product was obtained, m.p. 110-112°. The infra-

red spectrum showed an intense band at 1055 cm.$^{-1}$. Bellamy (50) assigns

a peak at about 1050 cm.$^{-1}$ to sulfoxides. The product was therefore

tentatively formulated as α-phenylethyl 2,6-dimethylphenyl sulfoxide.

The infrared spectrum of the crude reaction product did not show any

significant absorption in the region 1300 - 1350 cm.$^{-1}$ assigned to the

sulfone group (48).

Treatment of α-phenylethyl 2,6-dimethylphenyl sulfide with

hydrogen peroxide in acetic acid at room temperature gave the desired

product, α-phenylethyl 2,6-dimethylphenyl sulfone, in 46 per cent yield

m.p. 134.5 - 135.5°. The infrared spectrum showed strong absorption at

1310 and 1145 cm.$^{-1}$ as expected for the sulfone group (48). The n.m.r.

spectrum and analytical data were in accordance with the assigned

structure.

The rearrangement product of the substituted ester, α-(p-methoxy-

phenyl)ethyl 2,6-dimethylphenyl sulfone, was obtained from the reaction

between 2,6-dimethylbenzenesulfinic acid and α-(p-methoxyphenyl)ethanol

in formic acid containing sodium formate (29). The infrared spectrum

showed bands at 1315 and 1150 cm.$^{-1}$. The n.m.r. spectrum and analytical

data were in accordance with the assigned structure.

A summary of some physical properties of the esters and sulfones

is presented in Table III.

TABLE III

Properties of 2,6-dimethylbenzenesulfinates and sulfones

Compound (a)	M.p. $^{\circ}$C	Infrared absorption
R.O.SO.Ar	65.5-67.5	11.45μ (875 cm.$^{-1}$) in CHBr$_3$ 1135, 880 cm.$^{-1}$ in CS$_2$
R'.O.SO.Ar	69-71	1130, 865 cm.$^{-1}$ (11.6μ) in CS$_2$
R.SO$_2$.Ar	134.5-135.5	7.65μ (1310 cm.$^{-1}$) in CCl$_4$ 1310, 1145 cm.$^{-1}$ in CS$_2$
R'.SO$_2$.Ar	116-117	7.65μ (1310 cm.$^{-1}$) in CCl$_4$ 1315, 1150 cm.$^{-1}$ in CS$_2$

(a) R = α-phenylethyl, R' = α-(p-methoxyphenyl)ethyl,

Ar = 2,6-dimethylphenyl

Infrared Measurements

The fraction of sulfone formed in the reactions was determined by quantitative infrared measurements. Solutions of the sulfone in the appropriate solvent were prepared. After an extraction procedure, as used in the kinetic runs, the optical density of a solution prepared in a standard way was determined at 7.65μ . In the early work with both esters bromoform was used as the solvent for infrared measurements. Since bromoform absorbs in the region studied the intensity of the peaks is lower than in carbon tetrachloride which is optically clear in that region. Accordingly, later measurements were carried out in the latter solvent. From the measured optical density in a kinetic run the yield of sulfone was calculated by reading its concentration off a plot of optical density against concentration. A typical set of calibration results is

given in Table IV and the plots for both sulfones in Figures VII and VIII. Other sets of calibration results are given in the experimental section.

Figure VII shows that α-phenylethyl 2,6-dimethylphenyl sulfone obeys the Lambert-Beer Law in both solvents. The plots for α-(p-methoxyphenyl)ethyl 2,6-dimethylphenyl sulfone are not linear (Figure VIII). In practice the curves were approximated by two intersecting straight lines. Since the concentrations of sulfone obtained under the experimental conditions were less than 8×10^{-3} M and the curvature is small up to that concentration such a procedure should not lead to significant errors. The sulfone yields measured in the two solvents agreed within experimental error.

A plot similarly obtained for α-phenylethyl 2,6-dimethylbenzenesulfinate is shown in Figure IX. It is seen that this compound obeys the Lambert-Beer Law at concentrations up to 0.025 M. In kinetic runs the initial concentration of the ester was 0.020 to 0.030 M with a few exceptions.

Kinetics

The kinetics of the reaction of α-phenylethyl 2,6-dimethylbenzenesulfinate were studied by following the rate of disappearance of the ester. Since the optical density at 11.43μ is directly proportional to concentration the rate of disappearance of ester is equivalent to the rate of disappearance of the peak at 11.43μ, the quantity actually measured. The rate constants were calculated from the formula

$$kt = 2.303 \log D_o/D,$$
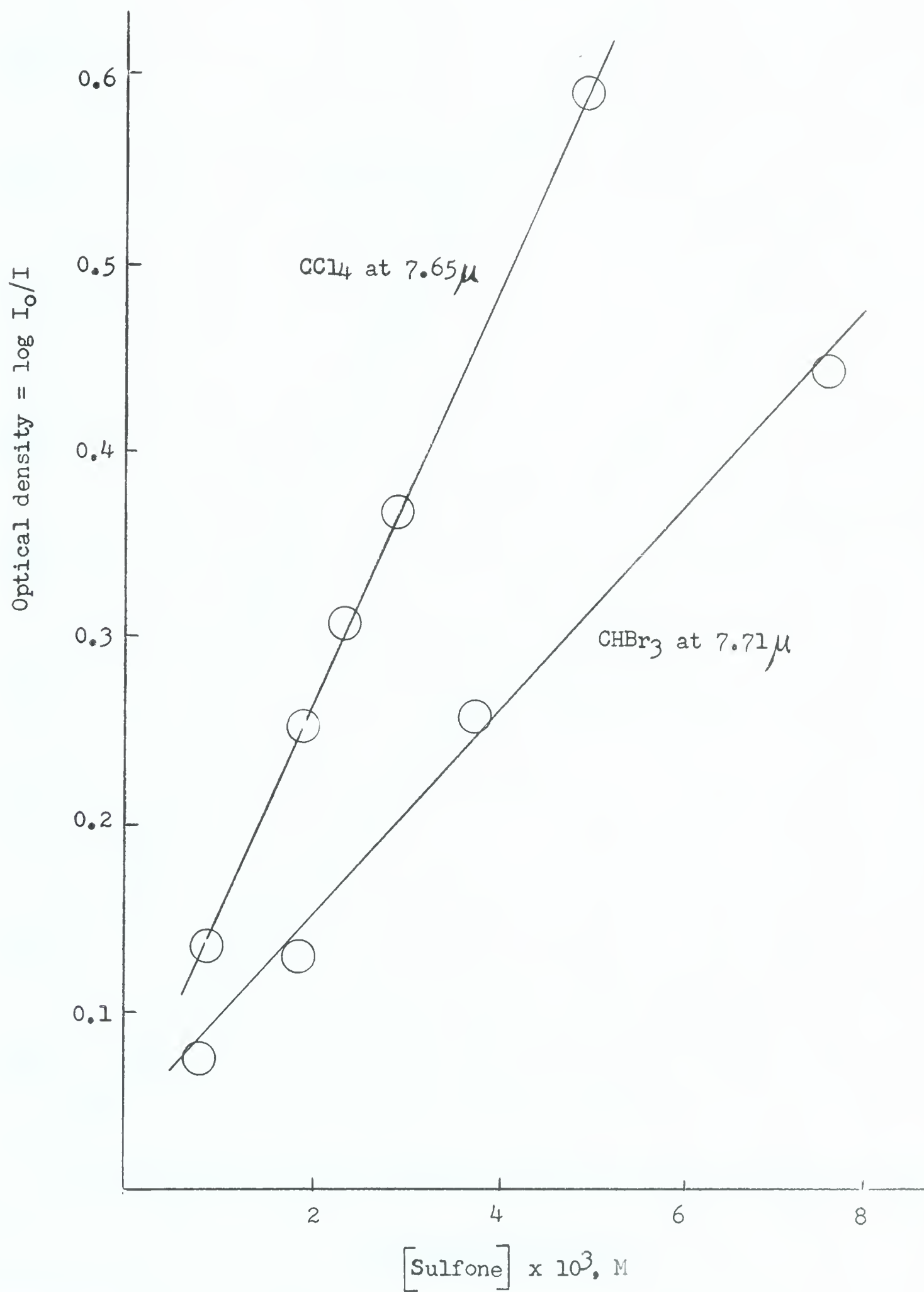
FIGURE VII

Lambert-Beer plot for α-phenylethyl 2,6-dimethylphenyl sulfone.

FIGURE VIII

Lambert-Beer plots for ⍺-(p-methoxyphenyl)ethyl 2,6-dimethylphenyl sulfone.
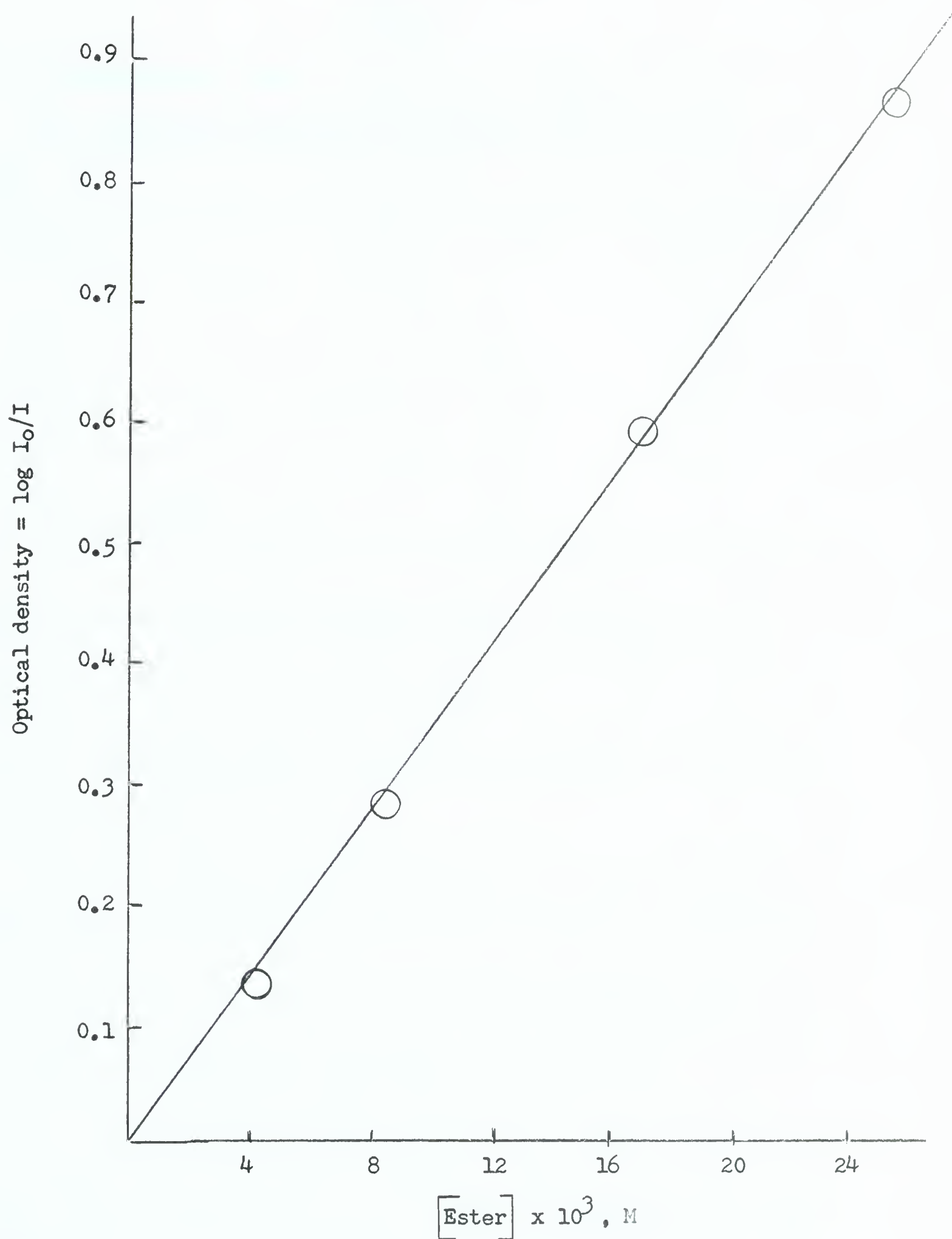
FIGURE IX

Lambert-Beer plot for ∝-phenylethyl 2,6-dimethylbenzenesulfinate in bromoform at 11.43μ.

TABLE IV

The relationship between optical density and concentration

for α-(p-methoxyphenyl)ethyl 2,6-dimethylphenyl sulfone

[Sulfone]	I_0/I(a)	log I_0/I
0.009462M	720/82	0.9435
.007570	816/120	.8325
.005677	869/177	.6910
.003785	855/291	.4781
.001892	925/492	.2741

(a)   In CCl_4 at 7.65μ .

where D is optical density at 11.43μ at time t.   In all runs in 60 volume per cent ethanol-water good first-order rate constants were obtained up to at least 75 per cent reaction.   None of the products of the reaction show significant absorption in that region.   A sample rate run is given in Table V.

The first runs carried out with this ester were followed by titrating the acid produced in the solvolysis reaction.   It was found that the amount of acid present in the solution at first increased and then slowly decreased, the maximum value being reached after four to six days.   The rate constants were calculated from the formula

$$kt = 2.303 \log (T_\infty - T_0)/(T_\infty - T),$$

where T is the titre at any time t. T_∞ was taken as the maximum titre obtained (after 4-6 days, i.e., 5-7 half-lives).   Sample runs are shown in Tables VI and VII.   The rate of disappearance of acid is seen to be

TABLE V

Spectrophotometric rate of disappearance of α-phenylethyl

2,6-dimethylbenzenesulfinate in 60% ethanol at 90° (a) (Run 1-184)

[Ester] = 0.02552M, [NaOAc] = 0.09404M

t(min)	$D = \log I_0/I$	$\log D_0/D$	$k \times 10^5, \sec^{-1}$
0	0.8773	--	--
278	.7141	0.0893	1.23
957	.4625	.2780	1.12
1723	.2586	.5305	1.18
2526	.1595	.7403	1.13
3895	.0654	1.2745	1.11
		Mean =	1.15 ± .04

(a) In all Tables 90° signifies 90.00 ± .03°

quite slow compared to its rate of appearance.

It was shown that the disappearance of acid was due to decomposition of 2,6-dimethylbenzenesulfinic acid. The results of a control run are shown in Table VIII. The decrease in acid titre is of the same order of magnitude as that observed during a kinetic run (compare Tables VI and VII).

The kinetics of the reaction of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate were followed by titrating the acid produced in the solvolysis. Since this ester is much more reactive than the unsubstituted ester no difficulties were encountered due to acid decomposition. The results of a control run showing the stability of the acid in ethanol at 70° (the conditions used in most of the work on this ester) are shown in Table IX. Reaction of the sulfinate ester is complete

TABLE VI

Rate of solvolysis of α-phenylethyl 2,6-dimethylbenzenesulfinate
in 60% ethanol at 90° (Run 1-118)

[Ester] = 0.0345M, [NaOAc] = 0.0596M, Calculated titre = 4.94 ml.

t(min.)	Titre (a)	$\log (T_\infty - T_0)/T_\infty - T)$	$k \times 10^5, \text{sec.}^{-1}$
0	0.654	--	--
30	0.901	0.0374	(4.76)
145	1.087	.0678	1.80
265	1.350	.1149	1.67
514	1.722	.1915	1.43
833	2.356	.3648	1.69
1305	2.552	.4362	1.28
2130	3.184	.8090	1.45
3061	3.414	1.1053	1.39
5275	3.578	--	--
8298	3.649 (b)		Mean = 1.53 ± .16
13428	3.570		
18605	3.515		
22753	3.373		

(a) Ml. of 0.03488M sodium methoxide required to neutralise 5 ml. of solution.

(b) T_∞ = 74% solvolysis.

TABLE VII

Rate of solvolysis of α-phenylethyl 2,6-dimethylbenzenesulfinate in 60% ethanol at 90° (Run 1-166)

[Ester] = 0.02912M, [NaOAc] = 0.1025M, calculated titre = 4.174 ml.

t(min.)	Titre	$\log(T_\infty - T_0)/T_\infty - T)$	$k \times 10^5, \sec^{-1}$
0	0.632 ml.	--	--
190	1.142	0.0816	1.65
497	1.697	0.1923	1.49
1224	2.506	0.4312	1.35
2220	3.170	0.8313	1.44
3142	3.283	0.9606	1.17
9694	3.609(a)	--	Mean = 1.42 ± .13
25936	3.059		
106517	2.054		

(a) T_∞ = 87% solvolysis

TABLE VIII

Stability of 2,6-dimethylbenzenesulfinic acid in 60% ethanol at 90°

[Acid] = 0.03166M, [NaOAc] = 0.09804M, calculated titre = 4.539 ml.

Time	Titre	Time	Titre
0	4.495 ml.	4 days	4.521 ml.
0	4.459	14 days	4.215
250 min.	4.513	42 days	3.479
3156 min.	4.503		

TABLE IX

Stability of 2,6-dimethylbenzenesulfinic acid in ethanol at 70°(a)

[Acid] = 0.02981M, [2,6-Lutidine] = 0.09649M, calculated titre = 4.273 ml.

Time	Titre	Time	Titre
0	4.173 ml	4 days	4.204 ml.
0	4.189	7 days	4.205
431 min.	4.216	22 days	4.214
1494 min.	4.183	44 days	4.553

(a) In all tables 70° signifies 70.00 ± .03°

in less than four hours under these conditions. A sample rate run on

α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate in ethanol at

70° is shown in Table X. The rate constant was calculated as for the

titrimetric rates on the unsubstituted ester. No attempt was made to

follow the reaction by the infrared method as the ester and products

of the reaction have a band about 830 cm^{-1} due to the 1,4-substituted

aromatic system (30), which interfere with measurement of the ester band

at 865 cm^{-1}

The rates of reaction of different mixtures of the two

diastereomers of α-phenylethyl 2,6-dimethylbenzenesulfinate are presented

in Table XI. It is seen that the rates of reaction of the two diastereom-

ers are similar but not equal. The fraction of rearrangement is very

similar and may be identical within experimental error.

The rate constant of the fast diastereomer can be estimated as

follows. It was first assumed that for a mixture of two diastereomers,

A and B, $[A] = 2[B]$, $k_A = 1.4 \times 10^{-5} sec^{-1}$, $k_B = 0.9 \times 10^{-5} sec^{-1}$.

TABLE X

Titrimetric rate of solvolysis of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate in ethanol at 70° (Run 2-14)

[Ester] = 0.02289M, [KOAc] = 0.02661M, calculated titre = 3.281 ml.

t(sec.)	Titre(ml.)	$\log(T_\infty - T_0)/(T_\infty - T)$	$k \times 10^4 \text{sec.}^{-1}$
0	0.335	--	--
120	.471	0.0314	6.02
240	.592	.0614	5.89
360	.703	.0909	5.81
540	.902	.1494	6.36
720	1.039	.1948	6.22
900	1.191	.2514	6.42
1080	1.302	.2979	6.35
1260	1.413	.3501	6.39
1440	1.525	.4099	6.54
1620	1.595	.4520	6.42
22 hrs.(∞)	2.276	--	--
22 hrs.(∞)	2.289 (a)	Mean =	$6.32 \pm .22$

(a) T_∞ = 2.283 ml.

Assuming that the initial optical density due to A is 0.500 and due to B is 0.300 the optical density due to each diastereomer at any time can be calculated. The initial optical density in most runs was about 0.8 and it is assumed here that B has a more intense band than A. In the second calculation the opposite is assumed. The initial intensities in a number

TABLE XI

The solvolysis and rearrangement of the diastereomeric

α-phenylethyl 2,6-dimethylbenzenesulfinates in 60% ethanol at 90°

Run	[Ester]	%FD(a)	[Base](b)	$k \times 10^5$,sec.$^{-1}$	$F_{rear.}$	$F_{solv.}$
2-151	0.02238M	0	0.09649M	0.87 ± .03	0.111	--
2.206	.02232	67	.09696	1.28 ± .15	.126	0.874
2-212	.02391	65	.09747	1.15 ± .09	.136	
				1.09 ± .04(c)		.868

(a) % Fast diastereomer

(b) 2,6-Lutidine

(c) Titrimetric rate constant

of runs showed that the two diastereomers have a band of approximately

equal intensity. The total optical density at the times at which points

were taken in Run 2-212 was calculated and from these numbers the apparent

calculated rate constant determined. The value obtained was $(1.19 \pm .01)$

$\times 10^{-5}$ sec.$^{-1}$. Similarly if it is assumed that $k_A = 1.8 \times 10^{-5}$ sec.$^{-1}$ and

that the initial optical densities are 0.600 and 0.250 respectively the

calculated apparent rate constant is $(1.48 \pm .03) \times 10^{-5}$ sec.$^{-1}$. The

observed values, allowing for experimental error, for such a mixture lie

between 1.04 and 1.43 $\times 10^{-5}$ sec.$^{-1}$ (Table XI) and hence the rate constant

for the fast diastereomer is probably between 1.2 and 1.9 $\times 10^{-5}$ sec.$^{-1}$. A

sample hypothetical rate calculation is given in the experimental section, p 139.

The rate constant observed for the pure diastereomer of

α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate in ethanol

containing 0.09649M 2,6-lutidine at 70° was $(5.63 \pm .16) \times 10^{-4} \text{sec}^{-1}$

(see Table XII). The yields of sulfone and solvolysis products were

28 and 72 per cent respectively. A run was carried out under the above

conditions using the mother liquors from the ester preparation, which,

as already reported, contained the two diastereomers in the ratio 80:20,

along with some impurities. The observed rate constant was $(8.01 \pm .12)$

$\times 10^{-4} \text{sec}^{-1}$. The yields of sulfone and solvolysis products were 21.7

and 59.4 per cent respectively. The ratio of these yields is 26.8:73.2.

As in the case of the unsubstituted ester it is seen that the diastereomers

have different rate constants but give the same products in approximately

the same ratio.

The rate constant for the fast diastereomer was estimated as

follows. Assuming $\left[A\right] = 4\left[B\right]$, $k_A = 8.6 \times 10^{-4} \text{sec}^{-1}$, $k_B = 5.6 \times 10^{-4} \text{sec}^{-1}$

and initial titre = 2.000 ml. a similar calculation to that described

for the unsubstituted ester gave a rate constant of $(7.94 \pm .03)$

$\times 10^{-4} \text{sec}^{-1}$. This is very close to the observed value and hence the

rate constant for the fast diastereomer under these conditions may be

estimated as ca. $8.7 \times 10^{-4} \text{sec}^{-1}$.

Some rate constants for both diastereomerically pure esters are

reported in Table XII. In Run 2-80 the rate constant quoted is only

very approximate. The values obtained were erratic and appeared to drift

downward as is not surprising in measuring a very slow rate when side

reactions may occur. The estimate may be inaccurate by a factor of

two. The sulfone yield was estimated from the optical density at 7.65μ

after 18 months (ca. two half-lives). In Run 2-82 the rate constant

reported is for the first half-life only. Subsequently a downward drift

TABLE XII

Rates of reaction of α-phenylethyl 2,6-dimethylbenzenesulfinate (A) and

α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate (B) in anhydrous

ethanol containing 2,6-lutidine (0.09649M)

Run	Temp $^{\circ}$C	Ester	[Ester]	k, sec.$^{-1}$	$F_{rear.}$
2-80	70	A	0.01682M	4×10^{-8}	0.025
2-28	70	B	.02313	$(5.63 \pm .16) \times 10^{-4}$	.28
2-82	90	A	.01330	$(2.6 \pm .2) \times 10^{-7}$	.05
2-86	90	B	.02287	$(3.07 \pm .04) \times 10^{-3}$	.27

was observed.

From the overall rate constants and the fractions of sulfone formed

the rate constants for solvolysis and rearrangement were calculated, e.g.,

$k_{rear.}$ in Run 2-82 = $k \times F_{rear.}$ = $2.6 \times 10^{-7} \times 0.05$ sec.$^{-1}$. These rate

constants, calculated from the data of Table XII and the relative rates

for each reaction of the two esters are listed in Table XIII. Rate

constants for the reactions in various solvents and in the presence of

2,6-dimethylbenzenesulfinic acid are given in Table XIV. It is seen

that except in ethanol 2,6-dimethylbenzenesulfinic acid has no effect

on the rate of reaction and that the reactions of both esters are

faster in aqueous ethanol than in ethanol.

Product Analysis

The products of the reaction of α-phenylethyl 2,6-dimethyl-

benzenesulfinate in 60 per cent ethanol and of α-(p-methoxyphenyl)ethyl

2,6-dimethylbenzenesulfinate in ethanol were also examined.

TABLE XIII

The relative rates of solvolysis and rearrangement of α-phenylethyl 2,6-dimethylbenzenesulfinate (A)
and α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate (B) in anhydrous ethanol.

Temp. °C	Ester	k_{solv}, sec.$^{-1}$	k_{rear}, sec.$^{-1}$	10^{-4} k_B / k_A		
				Total	Solv.	Rear.
70	A	4×10^{-8}	1×10^{-9}			
70	B	4.1×10^{-4}	1.6×10^{-4}	1	1	16
90	A	2.5×10^{-7}	1×10^{-8}			
90	B	2.4×10^{-3}	8.3×10^{-4}	1	1	8

TABLE XIV

The effect of solvent and of 2,6-dimethylbenzenesulfinic acid on the rate of reaction of α-phenyl-ethyl 2,6-dimethylbenzenesulfinate (A) and α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate (B).

Run	Ester	$\left[\text{Ester}\right]$	Solvent	Temp.°C	Base	$\left[\text{Base}\right]$	$\left[\text{ArSO}_2\text{H}\right]$(a)	$k \times 10^5$ sec.$^{-1}$
1-216	A	0.02527M	60%EtOH	90	NaOAc	0.3546M	—	0.98 ± .04
1-222	A	.02765	60%EtOH	90	NaOAc	.2518	0.08820M	1.05 ± .06
2-82	A	.01330	EtOH	90	2,6-L (b)	.09649	—	0.026 ± .002
2-28	B	.02313	EtOH	70	2,6-L	.09649	—	56.3 ± 1.6
2-38	B	.02338	EtOH	70	2,6-L	.09649	0.03071	73.5 ± 1.3
2-102	B	.02242	80%EtOH(c)	50(d)	2,6-L	.09649	—	129 ± 4
2-88	B	.02062	60%EtOH	25(e)	2,6-L	.09649	—	45.1 ± 1.1
2-89	B	.02097	60%EtOH	25	2,6-L	.09649	0.02138	45.7 ± 1.9

(a) 2,6-Dimethylbenzenesulfinic acid. (b) 2,6-lutidine.

(c) 80 volume % ethanol-water. (d) 50.00 ± .03°. (e) 25.00 ± .03°.

The ethanolysis product from α-phenylethyl 2,6-dimethyl-benzenesulfinate, α-phenylethyl ethyl ether, was synthesised by treatment of α-phenylethanol with powdered potassium (3) or preferably with sodium hydride (42) followed by reaction with ethyl bromide.

Gas liquid chromatography was examined as a possible method of analysis of the products from the reaction of α-phenylethyl 2,6-dimethyl-benzenesulfinate in 60 per cent ethanol. Perkin-Elmer Column K was used at 175°. Mixtures of α-phenylethanol, α-phenylethyl ethyl ether, styrene and acetophenone were prepared and injected. For the last three compounds the peak area relative to α-phenylethanol was plotted against the mole ratio relative to the same compound. In all cases a good straight line was obtained. Solutions of α-phenylethanol and α-phenylethyl ethyl ether in 60 per cent ethanol were prepared and analysed by gas liquid chromatography after an extraction procedure using methylene chloride. From the relative peak areas the mole ratio was obtained by using the above plots. The results of these experiments are reported in Table XV. It is seen that the alcohol:ether ratio can be measured with reasonable accuracy.

In two kinetic runs an infinity point was examined by g.l.c. using the same procedure as in the above experiments. Details of the conditions in these runs will be found in Table XVIII (Chapter II). In Run 2-149 the observed ROEt:ROH ratio was 0.527. A peak was also observed at the same retention time as styrene, corresponding to a styrene:ROH ratio of 0.089. Since 11.1 per cent yield of sulfone was measured spectrophotometrically the yields of α-phenylethanol, α-phenylethyl ethyl ether and styrene may be calculated as 55.0, 29.0

TABLE XV

Gas liquid chromatographic analysis of known mixtures of

α-phenylethanol and α-phenylethyl ethyl ether in 60% ethanol

Wt. of ROH(a)	Wt. of ROEt(b)	Mole ratio ROEt:ROH	
		Found	Calculated
0.1690 g.	0.1933 g.	0.850	0.846
.1821	.1403	.588	.626
.2802	.0784	.192	.207

(a) α-Phenylethanol

(b) α-Phenylethyl ethyl ether.

and 4.9 per cent respectively. In Run 2-151 the observed ratio of

ROEt:ROH was 0.534. Since 2,6-lutidine was present and it has approxi-

mately the same retention time as styrene the latter compound could not

be observed. In neither run was any acetophenone formed. Since

application of the extraction procedure developed during the work on

g.l.c. to actual product isolation was successful the former method of

analysis was not pursued further.

Details of the isolation procedure used for product analyses are

given in the experimental section. Two control runs using the same

procedure with known mixtures of α-phenylethanol, α-phenylethyl ethyl

ether and α-phenylethyl 2,6-dimethylphenyl sulfone are reported in

Table XVI. In the second run the solution was heated at 90° for ten

days, showing that the products are stable under the reaction condi-

tions. The results indicate that at least 85 per cent of each product

can be isolated by the procedure used.

TABLE XVI

Control isolation of α-phenylethanol, α-phenylethyl ethyl ether and α-phenylethyl 2,6-dimethyl-phenyl sulfone from 60% ethanol

Run	$ArSO_2R$(a)		ROH		ROEt		% Recovery of		
	Weighed	Found	Weighed	Found	Weighed	Found	$ArSO_2R$	ROH	ROEt
2-163	108 mg.	99 mg.	204 mg.	182 mg.	144 mg.	127 mg.	92	89	88
2-174 (b)	106	98	185	158	249	237	93	85	95

(a) α-Phenylethyl 2,6-dimethylphenyl sulfone

(b) 0.04848 M 2,6-lutidine present

TABLE XVII

Products from the reaction of α-phenylethyl 2,6-dimethylbenzenesulfinate

in 60% ethanol at 90°

Run	[Ester]	[2,6-Lutidine]	% Yield of		
			ArSO$_2$R	ROEt	ROH
2-161	0.03658M	0.09696M	11.5	30.0	50.5
2-162	.03742	.09696	12.7	29.6	46.4
2-170	.02934	.04848	11.7	35.5	44.2
2-231	.02643	.09747	12.6	28.2	39.7
2-232	.02677	.04874	--	29.9	43.3

The results of the isolation experiments are given in Table

XII. The product fractions were identified by their infrared and

nuclear magnetic resonance spectra. The ether fraction was examined

for the presence of styrene by gas liquid chromatography. Inconsistent

results were obtained, a compound with the same retention time as

styrene being absent in some cases and present in others. Since styrene

was not detectable in the infrared, it is considered likely that the

g.l.c. peak is not in fact due to a reaction product.

The mean value of the sulfone yield from Table XVII is (12.1 ± 0.5)

per cent in good agreement with the values obtained by infrared measure-

ments (see Tables XI and XVIII). The reproducibility of the yields of

solvolysis products is only fair but the mean values of 30.6 per cent

α-phenylethyl ethyl ether and 44.8 per cent α-phenylethanol are in rough

agreement with the values obtained by gas liquid chromatography. The

greatest error appears to be in the yield of alcohol. In control run

2-174, 15 per cent of the alcohol was lost and such loss is not

surprising as α-phenylethanol is appreciably soluble in water. In any case about 90 per cent of the reaction products are accounted for.

There was no evidence of the formation of ethyl 2,6-dimethyl-benzenesulfinate from α-phenylethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol. In ethanol good first-order rate constants were not obtained by following the rate of disappearance of the α-phenylethyl ester, a downward drift in rate constant being observed both at 70 and 90°. Since the ethyl ester absorbs in approximately the same region (2) formation of the ethyl ester might account for the downward drift observed.

The products from the reaction of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate in ethanol at 70° were also isolated. A solution of the ester and potassium acetate in ethanol was allowed to react for ten half lives and the product mixture isolated. It was found that α-(p-methoxyphenyl)ethyl 2,6-dimethylphenyl sulfone could be crystallised from the product mixture by addition of small amounts of pentane. The sulfone was obtained in 29.4 per cent yield by weight. It was identified by its infrared spectrum and melting point. Removal of the pentane from the mother liquors gave an oil corresponding to a 72.1 per cent yield of α-(p-methoxyphenyl)ethyl ethyl ether (by weight). The structure was assigned on the basis of the infrared spectrum (strong band at 1090 cm.$^{-1}$) and the nuclear magnetic resonance spectrum. No sulfone was apparent in the infrared spectrum. The same product, along with minor impurities, was obtained from the solvolysis of α-(p-methoxyphenyl)ethyl bromide.

These values are in good agreement with other methods of measurement.

The mean value of the sulfone yield measured by the infrared method is 28.7 per cent (see Tables XII, XXIII and XXV). Titration of the acid produced in the solvolysis reaction in ethanol gave a mean value for α-(p-methoxyphenyl)ethyl ethyl ether formation of 69.7 per cent. The details of these results are more conveniently reported in the following chapter (see Tables XXIII and XXV).

DISCUSSION

Three possible modes of reaction of sulfinate esters are illustrated below. The discussion in this chapter is directed to showing that the reactions studied were ionisation reactions and not acid or base catalysed.

Base catalysis

$$Ar.SO.OR + B^- \longrightarrow Ar.SO.B + RO^-$$

$$Ar.SO.B + R'OH \longrightarrow Ar.SO.OR' + HB$$

where R' = H or Alkyl, R'OH = solvent.

Acid catalysis

$$H^+ + Ar.SO.OR + R'OH \longrightarrow Ar.SO_2.R + Ar.SO_2H + ROR' + H^+$$

$$\underline{or} \; Ar.SO.OR' + ROH + H^+$$

Ionisation

$$Ar.SO.OR \longrightarrow Ar.SO_2^- + R^+$$

$$Ar.SO_2^- + R^+ \longrightarrow Ar.SO_2.R$$

$$R^+ + R'OH \longrightarrow ROR' + H^+$$
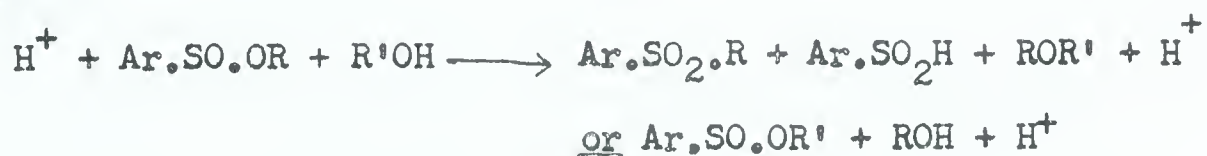
The base catalysed reaction of a number of sulfinate esters has

-47-

been studied by Bunton (9) and in this laboratory (2). Noreyko found

that p-methoxyneophyl 2,6-dimethylbenzenesulfinate reacted in ethanol,

buffered with 2,6-lutidine, with a rate constant of 6 x 10^{-9} sec.$^{-1}$ at

90°, and in 60 per cent ethanol at 90° with a rate constant of

7 x 10^{-8} sec.$^{-1}$. In ethanol the product was ethyl 2,6-dimethylbenzene-

sulfinate (2). The rapid formation of ethyl o-nitrobenzenesulfinate

from α-phenylethyl o-nitrobenzenesulfinate in ethanol indicates that

sulfur-oxygen bond cleavage, catalysed by acetate ion, is the preferred

mode of reaction for that compound. Similar results have been obtained

for other ortho-substituted benzenesulfinates (18). Herbrandson and

Cusano (31) have studied the reaction of the two diastereomeric

(-)-menthyl p-iodobenzenesulfinates with ethoxide ion in ethanol. The

esters reacted completely by sulfur-oxygen bond cleavage to yield

(-)-menthol and ethyl p-iodobenzenesulfinate. The ethyl ester was

found to be optically inactive, but since optically active ethyl ester

was not prepared it is not clear whether this inactivity is due to

formation of racemic ester or to a low specific rotation for the ethyl

ester. Since the initial formation of ethyl ester would produce inver-

sion at the asymmetric sulfur atom, it would be expected that the ethyl

ester first formed would be optically active. Racemic ethyl ester

formation would require attack by ethoxide ion on the ethyl ester. If

the ethyl ester formed in the reaction is racemic it therefore follows

that the ethyl ester must be more reactive than the menthyl ester. This

could be generalised by saying that a primary sulfinate is more suscep-

tible to sulfur-oxygen bond cleavage than a secondary sulfinate. This

is supported by the fact that p-methoxyneophyl 2,6-dimethylbenzenesulfinate

reacts with ethoxide ion in ethanol twice as fast as does the corresponding isopropyl ester (2). However if this effect is due to an inductive effect on the basicity of the leaving group such a generalisation would not apply to α-phenylethyl sulfinates as the phenyl group is electron withdrawing. However, Bunton and Hendry (9) found that the rate of sulfur-oxygen bond cleavage by hydroxyl ion in 60 per cent aqueous dioxane was twice as fast for methyl p-toluenesulfinate as for benzhydryl p-toluenesulfinate. The best approximation that can be made is that sulfur-oxygen bond cleavage in α-phenylethyl sulfinates should occur at approximately the same rate as for the corresponding p-methoxy-neophyl esters under the same conditions.

Of the esters and conditions studied, sulfur-oxygen bond cleavage under solvolytic conditions is most likely to occur in the reaction of α-phenylethyl 2,6-dimethylbenzenesulfinate in ethanol, i.e., the reaction of the least reactive ester in the poorest ionising solvent. In this case formation of ethyl 2,6-dimethylbenzenesulfinate cannot be definitely ruled out. However, the observed rate of reaction in ethanol is 2.6×10^{-7} sec.$^{-1}$ at 90°, 50 times faster than the observed rate for p-methoxyneophyl 2,6-dimethylbenzenesulfinate under the same conditions. Since the rates of sulfur-oxygen bond cleavage in the two compounds should be approximately equal, as discussed above, it is therefore considered likely that even in these extreme circumstances sulfur-oxygen bond cleavage is of minor importance. In any case, as will be seen below, the rate constants obtained under these conditions are required only as a measure of the maximum possible rate of carbon-oxygen bond cleavage.

The solvolysis of α-phenylethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol gives about 30 per cent α-phenylethyl ethyl ether. It is not possible for this compound to be formed by sulfur-oxygen bond cleavage and it must be formed by carbon-oxygen bond cleavage. Under these conditions α-phenylethanol could conceivably be formed by either sulfur-oxygen or carbon-oxygen bond cleavage. In Runs 2-206 and 2-212 (Table XI) the sum of the sulfone and acid yields was 100.0 and 100.4 per cent respectively. Since sulfur-oxygen bond cleavage would be expected to yield ethyl 2,6-dimethylbenzenesulfinate as well as 2,6-dimethylbenzenesulfinic acid, the quantitative yield of sulfone and acid indicates that sulfur-oxygen bond cleavage is not an important mechanism of formation of α-phenylethanol under these conditions. Also, the observed rate of reaction of α-phenylethyl 2,6-dimethylbenzene-sulfinate in 60 per cent ethanol is 1×10^{-5} sec.$^{-1}$ whether 2,6-lutidine or sodium acetate is the added base. This is 140 and 20 times as fast as the rate of reaction of p-methoxyneophyl 2,6-dimethylbenzenesulfinate under comparable conditions (2). Thus on the basis of both kinetic and product data sulfur-oxygen bond cleavage under these conditions can be ruled out.

The solvolysis of α-(p-methoxyphenyl)ethyl 2,6-dimethyl-benzenesulfinate in ethanol gives only α-(p-methoxyphenyl)ethyl 2,6-dimethylphenyl sulfone and α-(p-methoxyphenyl)ethyl ethyl ether. Ether formation is accompanied by the production of acid. None of these products could conceivably be formed by sulfur-oxygen bond cleavage, but are the expected products from carbon-oxygen bond cleavage.

The equilibration of diastereomers in pyridine appears to occur by

sulfur-oxygen bond cleavage. Inversion about sulfur by molecular
vibration without bond cleavage, in a manner analogous to that occurring
in ammonia or amines, is possible. On this basis it is however diffi-
cult to account for the fact that the interconversion occurs more
readily in the presence of acid. Any mechanism involving carbon-oxygen
bond cleavage would be expected to be very sensitive to the methoxy-
substituent, but the observed rates of equilibration of the substituted
and unsubstituted esters are approximately equal. Carbon-oxygen bond
cleavage might also be expected to give sulfone, which was not one of the
observed products. Thus carbon-oxygen bond cleavage can be ruled out as
a mechanism for the equilibration. Sulfur-oxygen bond cleavage would
be expected to be relatively insensitive to the substituent as is ob-
served. The mechanism below is favored for the equilibration reaction.

$$
\text{Ar.S} \uparrow^{O} \text{—OR} + H^+ \quad \rightleftharpoons \quad \text{Ar.S} \uparrow^{O} \text{—}\overset{+}{\underset{H}{\text{OR}}}
$$

$$
\text{Ar.S} \uparrow^{O} \text{—}\overset{+}{\underset{H}{\text{OR}}} + N \quad \rightleftharpoons \quad \text{Ar.S} \uparrow^{O} \underset{N^+}{\big|} + ROH
$$

$$
\text{Ar.S} \uparrow^{O} \underset{N^+}{\big|} + N \quad \rightleftharpoons \quad \text{Ar.S} \overset{N^+}{\underset{\downarrow O}{\big|}} + N
$$

$$
\text{Ar.S} \overset{N^+}{\underset{\downarrow O}{\big|}} + ROH \quad \rightleftharpoons \quad \text{Ar.S} \underset{\downarrow O}{\big|} \text{—OR} + H^+ + N
$$
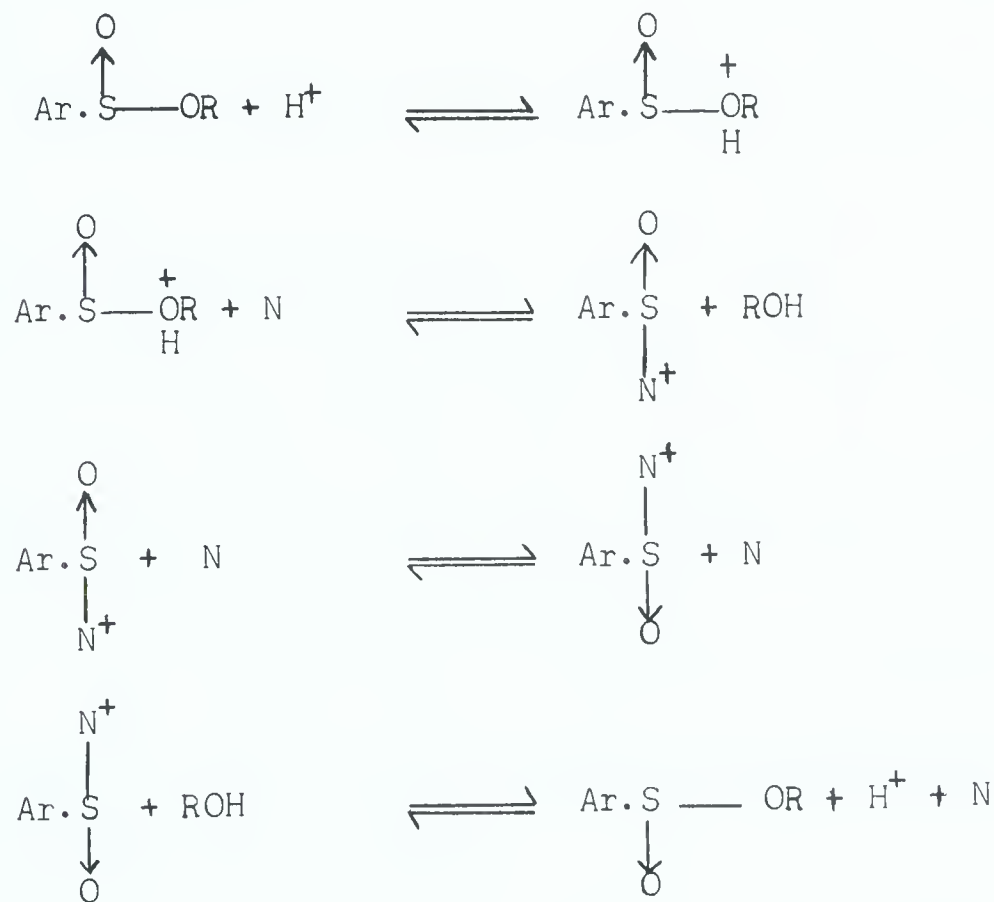
The nucleophile N in the second and third steps could be either
pyridine or bromide ion, since the results are not clear as to whether

bromide ion catalysis occurs. It is however most probably bromide ion

as that ion is known to be very nucleophilic towards the sulfur of

sulfinate esters (73). The fact that the same mixture of diastereomers

is obtained under different conditions and when the equilibrium is

approached from both sides, together with the equality of the equilibra-

tion rates from both sides, indicates that an equilibrium is in fact

established, despite the accompanying decomposition.

Since at the start of the reaction of the esters in ethanol and

aqueous ethanol there is little, if any, acid present an acid catalysed

reaction should give rise to auto-catalysis as observed by Bunton for

benzhydryl p-toluenesulfinate (9). In the presence of sodium acetate,

potassium acetate or 2,6-lutidine this was not observed. Also, when

2,6-dimethylbenzenesulfinic acid (in the presence of excess base) was

added at the start of the reaction (Table XIV) no increase in the rate

of reaction was observed for either ester in 60 per cent ethanol and

the increase observed in the rate of reaction of α-(p-methoxyphenyl)-

ethyl 2,6-dimethylbenzenesulfinate in ethanol was of the order expected

for a simple salt effect (see effect of other salts in Table XXV). The

rate of an acid catalysed reaction under these conditions should be

significantly increased. Thus an acid catalysed reaction if it occurs

at all is of very minor importance.

That the reactions do indeed occur by ionisation of the esters

is shown by the products of the solvolysis reaction (discussed above)

and by the kinetic evidence.

No attempt was made to obtain a quantitative correlation of the

rates of the reactions with the ionising power of the solvent, but it is

clear from the data of Table XIV that the effect of the solvent is

qualitatively as would be predicted for an ionisation reaction (59)

i.e., the reaction proceeds faster in ethanol-water than in ethanol.

α-Phenylethyl 2,6-dimethylbenzenesulfinate reacts faster in 60 per

cent ethanol than in ethanol at 90° by a factor of 40 (Table XIV).

The factor is 350 for α-phenylethyl chloride in the same solvents at

50° (45). In the related systems, cumyl 2,6-dimethylbenzenesulfinate and

benzhydryl 2,6-dimethylbenzenesulfinate, linear correlations of the rates

of solvolysis and rearrangement with the rates of solvolysis of

α-phenylethyl chloride and benzhydryl chloride respectively in various

solvents have been obtained (34,35).

The rate of reaction of α-($\underline{p}$-methoxyphenyl)ethyl 2,6-dimethyl-

benzenesulfinate in ethanol at 70 and 90° is faster by four powers of

ten than that of the unsubstituted ester (Table XIII). This is of the

order expected for an ionisation reaction, e.g., 2-($\underline{p}$-methoxyphenyl)-2-

propyl chloride solvolyses 3360 times faster than the unsubstituted

compound in 90 per cent acetone at 25° (32). The relative rate of 10^4

corresponds to a reaction constant (ρ) in the Hammett Equation (33) of

-15 (versus σ) or -5 (versus σ^+). These factors support the ionic

nature of the overall reaction. If some sulfur-oxygen bond cleavage

occurs in the reaction of α-phenylethyl 2,6-dimethylbenzenesulfinate

in ethanol the rate of carbon-oxygen bond cleavage would be less than

the measured rate of ester disappearance. In this case the effect of

the substituent would be even greater than 10^4 and the above argument

is unaffected.

The rearrangement reaction yielding sulfone could conceivably

occur by ionisation followed by combination of a carbonium ion and a

sulfinate ion or by a concerted, cyclic, relatively non-polar reaction.

A polar five-membered cyclic rearrangement of allylic sulfinates to

sulfones has been observed to occur (36). If the rearrangement of the

sulfinate esters studied in this work involved a three-membered cyclic

transition state the rate of rearrangement would be expected to be less

sensitive to substituent effects than an ionisation reaction. Table

XIII shows that the rearrangement reaction is one power of ten more

sensitive to the presence of a methoxy substituent than is either the

overall reaction or the solvolysis. It has been already concluded that

the overall reaction is ionic in nature and because of the larger

sensitivity of the rearrangement to the substituent it must also

involve ionic intermediates.

CHAPTER II

THE NATURE OF THE INTERMEDIATES IN THE REARRANGEMENTS AND

SOLVOLYSIS OF α-ARYLETHYL 2,6-DIMETHYLBENZENESULFINATES

RESULTS

The Solvolysis and Rearrangement of α-Phenylethyl 2,6-Dimethyl-

benzenesulfinate in 60 per cent Ethanol at 90°

The results of a series of kinetic runs on α-phenylethyl

2,6-dimethylbenzenesulfinate in 60 per cent ethanol at 90° are reported

in Table XVIII. In the first four runs the reaction was followed by

titrating the acid produced and, as already discussed in Chapter I, this

is not the best method due to decomposition of 2,6-dimethylbenzene-

sulfinic acid. All subsequent runs were followed by measuring the rate

of disappearance of the ester at 11.45μ. Some sample rates have been

given in Chapter I and two more are reported in Tables XIX and XX. The

rate constants obtained are somewhat erratic. At the time when most of

this work was done nuclear magnetic resonance facilities were not

available and the purification procedure described in Chapter I had not

been worked out. The ester samples used most likely were mixtures of

diastereomers in most of the runs. The melting points of some of the

ester samples are listed in Table XVIII. Melting points are however a

poor criterion of purity as may be seen from the data of Table XXXVI

which show that mixtures of diastereomers of widely varying composition

have practically the same melting point. Pure diastereomer was used in

Run 2-151 and in Run 2-149 the ester consisted of 74 per cent of the fast

diastereomer. In Run 1-118 the ester used was non-crystalline. Since

the two diastereomers react at different rates a variable fraction of

the fast diastereomer would give rise to variable observed rates of

reaction.

The sum of F_{solv} in Runs 154 and 166 and F_{rear} is close to unity

as expected. These values of F_{solv} are also in agreement with those

obtained from two known mixtures of the diastereomers (Table XI).

The rate constant and fraction of sulfone formed are seen to be

essentially unchanged by a change in the base present (Runs 2-149 and

2-151), by the presence of lithium perchlorate (Run 1-226) or by sodium

2,6-dimethylbenzenesulfinate (Run 1-222) except for a small salt effect

in the case of lithium perchlorate. In Runs 1-186, 214, 216, 222 and

226 sulfone formation was also followed. The rate constants were less

accurate than those obtained by following the rate of ester disappear-

ance but agreed within 30 per cent. Within experimental error they were

constant over the range of reaction followed. Two samples are given in

Tables XXI and XXII.

The Solvolysis and Rearrangement of α-(p-methoxyphenyl)ethyl

2,6-dimethylbenzenesulfinate in Ethanol and 60 per cent Ethanol

Most of the work with this ester was done in ethanol at 70° and

the bases added were potassium acetate and 2,6-lutidine which were

used as anhydrous stock solutions in ethanol. The reaction was followed

by titration of the acid produced in the solvolysis and the sulfone

yield was measured by the infrared method. The results of experiments

TABLE XVIII

The solvolysis and rearrangement of α-phenylethyl 2,6-dimethyl-

benzenesulfinate in 60% ethanol at 90°

Run	[Ester]	[NaOAc]	$k \times 10^5, \text{sec.}^{-1}$	$F_{solv.}$	$F_{rear.}$
1-118	0.0345M	0.0596M	$1.53 \pm .16$	0.74	
1-128	.02217(a)	.06155	$1.28 \pm .07$	.94	
1-154	.02899	.1010	$1.46 \pm .06$	.85	
1-166	.02912	.1025	$1.42 \pm .13$	.86	
1-184	.02552(b)	.09404	$1.15 \pm .04$		
1-186	.02716(c)	.1696	$1.20 \pm .10$		0.12
1-214	.02961	.03939	$1.17 \pm .06$		.13
1-216	.02527	.3546	$0.98 \pm .04$		.11
1-222(d)	.02765	.2518	$1.05 \pm .06$		.13
1-226(e)	.02683	.03541	$1.51 \pm .08$		.13
2-149	.02099(f)	.1084(g)	$1.02 \pm .07$		.11
2-151	.02238(h)	.09649(i)	$0.87 \pm .03$		.11

(a) M.p. 66-67°.

(b) M.p. 62-65°.

(c) M.p. 25-68°.

(d) 0.09920M 2,6-Dimethylbenzenesulfinic acid added.

(e) 0.1734M Lithium perchlorate added.

(f) M.p. 35-37°.

(g) Potassium acetate.

(h) M.p. 65.5-67.5°.

(i) 2,6-Lutidine.

TABLE XIX

Rate of disappearance of α-phenylethyl 2,6-dimethylbenzenesulfinate

in 60% ethanol at 90° (Run 1-214)

$[\text{Ester}] = 0.02961M, \quad [\text{NaOAc}] = 0.03939M$

t(min.)	$D = \log I_0/I$	$\log D_0/D$	$k \times 10^5, \text{sec.}^{-1}$
0	1.008	--	--
70	0.9619	0.0202	1.11
292	.8202	.0894	1.18
489	.6839	.1683	1.32
816	.5850	.2361	1.11
1456	.3501	.4591	1.21
2054	.2368	.6289	1.18
2856	.1538	.8164	1.10
		Mean =	$1.17 \pm .06$

TABLE XX

Rate of disappearance of α-phenylethyl 2,6-dimethylbenzenesulfinate

in 60% ethanol at 90° in the presence of 2,6-dimethylbenzenesulfinic acid

(Run 1-222)

$[\text{Ester}] = 0.02765M, \quad [\text{NaOAc}] = 0.2518M, \quad [\text{Acid}] = 0.08820M$

t(min.)	$D = \log I_0/I$	$\log D_0/D$	$k \times 10^5, \text{sec.}^{-1}$
0	0.7486	--	--
222	.6597	0.0549	0.95
730	.4852	.1884	0.99
1115	.3409	.3419	1.18
1559	.2748	.4352	1.07
2361	.1687	.6472	1.05
		Mean =	$1.05 \pm .06$

TABLE XXI

Rate of rearrangement of α-phenylethyl 2,6-dimethylbenzenesulfinate

in 60% ethanol at 90° (Run 1-186)

$[\text{Ester}] = 0.02716M$, $[\text{NaOAc}] = 0.1696M$

t(min.)	$D = \log I_0/I(7.7\mu)$	$\log(D_\infty - D_0)/(D_\infty - D)$	$k \times 10^5$ sec.$^{-1}$
0	0.0199	--	--
351	.0664	0.1146	1.25
1078	.1196	.2988	1.07
1740	.1875	.7849	1.73
2820	.1969	.9310	1.25
20 days (∞)	.2204	--	Mean = 1.33 ± .21

TABLE XXII

Rate of rearrangement of α-phenylethyl 2,6-dimethylbenzenesulfinate

in 60% ethanol at 90° (Run 1-214)

$[\text{Ester}] = 0.02961M$, $[\text{NaOAc}] = 0.03939M$

t(min.)	$D = \log I_0/I$	$\log(D_\infty - D_0)/(D_\infty - D)$	$k \times 10^5$ sec.$^{-1}$
0	0.0182	--	--
70	.0257	0.0139	0.76
292	.0478	.0577	0.76
489	.0571	.0775	0.61
816	.0933	.1649	0.77
1456	.1343	.2911	0.77
2054	.2048	.6676	1.25
2856	.2166	.7816	1.05
4383	.2492	1.5499	1.36
7402	.2386	1.1380	0.59
8 days (∞)	.2559	--	Mean = 0.88 ± .23

using these two bases are presented in Table XXIII. A sample rate with

potassium acetate was given in Table X and Table XXIV reports one with

2,6-lutidine as added base.

Potassium acetate is seen to have a small positive salt effect

on the rate of reaction and lutidine a slight depressing effect as would

be expected from their influence on the ionising power of the medium (65).

The variation of the reaction rate with base concentration is illustrated

in Figure X.

The effect of some salts on the reaction was also studied and

these results are listed in Table XXV. The effect of lithium perchlorate

is illustrated in Figure X and a sample rate with this salt is given in

Table XXVI. Added lithium perchlorate has a rate enhancing effect about

ten times greater than potassium acetate but has no effect on the products

of the reaction. The equation

$$k/k_o = 1 + b \left[Salt \right],$$

where k_o is the rate constant in the absence of salt, k is the rate

constant in the presence of salt and b represents the percentage increase

in rate per 0.01M salt, has been suggested for the correlation of salt

effects on rate constants (13). The b values for potassium acetate and

lithium perchlorate are 1.42 ± .05 and 13.5 ± 2.3 respectively. These

values are of the magnitude expected for a normal salt effect, e.g., in

the ethanolysis of 2-(2,4-dimethoxyphenyl) ethyl p-bromobenzenesulfonate

at 50° lithium perchlorate has a b value of 5.0 (74). At least in

acetolysis reactions, secondary systems are known to give larger salt

effects than primary systems and acetates to give smaller salt effects

than lithium perchlorate (74). The data are not sufficiently complete to

TABLE XXIII

Effect of base concentration on the reaction of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate

in ethanol at 70°.

Run	[Ester]	Base	[Base]	$k \times 10^4$, sec.$^{-1}$	$F_{rear.}$	$F_{solv.}$
2-14	0.02289M	KOAc	0.02661M	6.23 ± .22	0.25	0.71
2-22	.02423	KOAc	.1064	6.94 ± .21	.33	.69
2-20	.02306	KOAc	.2129	7.73 ± .14	.31	.69
2-28	.02313	2,6-L (a)	.09649	5.63 ± .16	.28	.68
2-30	.02298	2,6-L	.1930	5.13 ± .13	.265	.70

(a) 2,6-Lutidine.

TABLE XXIV

Rate of solvolysis of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzene-

sulfinate in ethanol at 70° (Run 2-28)

[Ester] = 0.02313M, [2,6-Lutidine] = 0.09649M, Calculated titre = 3.048 ml.

t(sec.)	Titre(ml.)	$\log(T_\infty - T_0)/(T_\infty - T)$	$k \times 10^4 \text{sec.}^{-1}$
0	0.159	--	--
120(a)	0.261	--	--
240	0.395	0.0309	5.92
360	0.452	.0451	(4.32)
480	0.559	.0725	(4.63)
660	0.738	.1226	5.22
840	0.913	.1780	5.69
1020	1.023	.2168	5.54
1200	1.131	.2586	5.51
1380	1.251	.3103	5.66
1560	1.369	.3680	5.87
1800	1.451	.4131	5.66
4 hours (∞)	2.190		Mean = 5.63 $\pm$ .16
24 hours (∞)	2.209(b)		

(a) Taken as zero time in the rate calculation.

(b) T_∞ = 2.200 ml. (72%).
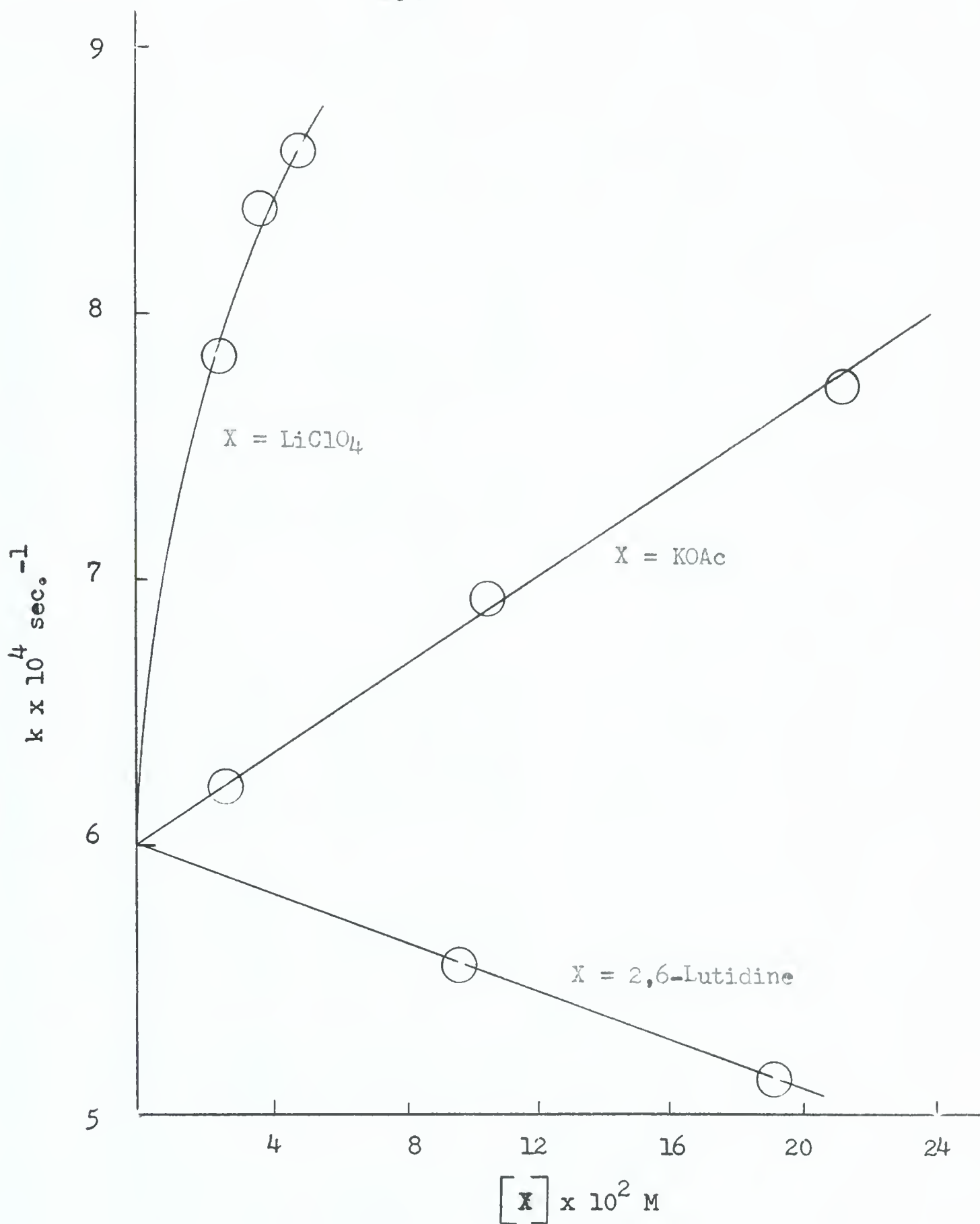
FIGURE X

The effect of addends on the rate of reaction of α-(p-methoxyphenyl)ethyl
2,6-dimethylbenzenesulfinate in ethanol at 70° (taken from Tables XXIII
and XX V).

TABLE XXV

The effect of added salts on the reaction of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate in ethanol at 70°.

Run	[Ester]	[2,6-Lutidine]	Salt	[Salt]	$k \times 10^4$, sec.$^{-1}$	Frear	Fsolv.
2-28	0.02313M	0.09649M	-	-	5.63 ± .16	0.28	0.66
2-38	.02338	.09649	ArSO$_2$H (a)	0.03071M	7.35 ± .13	.295	.71
2-40	.02325	.09649	LiClO$_4$	.02440	7.86 ± .19	.285	.72
2-72	.02343	.09649	LiClO$_4$	.03863	8.39 ± .11	.285	.72
2-70	.02086	.08684	LiClO$_4$	.04917	8.63 ± .25	-	-
2-99	.02116	.09649	NaN$_3$	.01704	6.56 ± .33	.285	.685 (b)

(a) 2,6-Dimethylbenzenesulfinic acid.

(b) Ca. 3% α-(p-methoxyphenyl)ethyl azide also formed.

TABLE XXVI

Solvolysis of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate

in ethanol at 70° in the presence of lithium perchlorate (Run 2-72)

[Ester] = 0.02343M, [2,6-Lutidine] = 0.09649M, [LiClO$_4$] = 0.03863M,

Calculated titre = 3.359 ml.

t(sec.)	Titre (ml.)	$\log(T_\infty-T_0)/(T_\infty-T)$	$k \times 10^4$, sec.$^{-1}$
0	0.225	--	--
60(a)	0.301	--	--
180	0.466	0.0359	(6.88)
300	0.670	.0848	8.13
660	1.136	.2227	8.54
780	1.232	.2574	8.22
900	1.372	.3138	8.59
1020	1.451	.3491	8.36
1140	1.543	.3942	8.40
1320	1.661	.4600	8.40
1500	1.770	.5310	8.47
152 min.	2.378		Mean = 8.39 ± .11
(∞)	2.388(b)		

(a) Taken as zero time in the rate calculation.

(b) T_∞ = 2.383 ml. (72%).

indicate whether the apparent curvature in the plot of rate constant against lithium perchlorate is real or not. A non-linear plot would not necessarily be abnormal as the linear relationship often observed is purely empirical (13). The addition of 2,6-dimethylbenzenesulfinic acid does not affect the yield of sulfone within experimental error and a salt effect for lutidinium 2,6-dimethylbenzenesulfinate somewhat less (b = 10.5) than that of lithium perchlorate is reasonable. Sodium azide is only sparingly soluble in anhydrous ethanol but even at the low concentration used some α-(p-methoxyphenyl)ethyl azide was formed. More extensive experiments on the effect of azide ion in 80 per cent ethanol are reported below.

The solvolysis and rearrangment of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol at 25° with and without added 2,6-dimethylbenzenesulfinic acid was also investigated. The results are reported in Table XXVII. It is seen that the rate of reaction and the yield of sulfone are unchanged by the presence of 2,6-dimethylbenzenesulfinate ion.

Solvolysis of bromides in the presence of sulfinate ion

α-Phenylethyl bromide was prepared from styrene and hydrogen bromide in acetic acid (37) and allowed to react in 60 per cent ethanol at 90° in the presence of sodium acetate (0.09057M) and 2,6-dimethyl-benzenesulfinic acid (0.02727M) for two minutes. At 25° in the same solvent a solvolysis rate constant of 1.75×10^{-3} sec.$^{-1}$ has been reported (38) and the half life at 90° can be estimated as less than one second. Thus complete reaction must have occurred in the time allowed. This was confirmed by titrating the acid produced. The

TABLE XXVII

The solvolysis and rearrangement of α-(p-methoxyphenyl)ethyl

2,6-dimethylbenzenesulfinate in 60% ethanol at 25°

Run	$\left[\text{Ester}\right]$	$\left[\text{2,6-L}\right]$(a)	$k \times 10^4 \text{sec.}^{-1}$	F_{solv}	F_{rear}
2-87	0.01939M	0.09649M	$4.89 \pm .57$	0.66	0.35
2-88	.02062	.09649	$4.51 \pm .11$	.66	.36
2-89(b)	.02097	.09649	$4.57 \pm .19$	.67	.335

(a) 2,6-Lutidine.

(b) 0.02138M 2,6-Dimethylbenzensulfinic acid added.

experimental value was 99 per cent of that calculated from the molarities

of the bromide and sulfinic acid present at the start of the reaction.

The optical density at 7.65μ (CCl_4) corresponded to a sulfone yield of

less than 0.4 per cent. α-Phenylethanol, which the total infrared

spectrum revealed to be the major component of the product mixture, has

a weak peak in that region. Thus 0.4 per cent represents an upper

limit for the yield of sulfone obtained in this experiment.

α-(p-Methoxyphenyl)ethyl bromide was prepared from the alcohol

and hydrogen bromide in benzene and allowed to react in ethanol at 25°

in the presence of 2,6-lutidine (0.01909M) and 2,6-dimethylbenzene-

sulfinic acid (0.01909M) for 85 minutes. Under similar conditions

α-phenylethyl bromide has a solvolysis rate constant of $6 \times 10^{-6}\text{sec.}^{-1}$

(38). Assuming that the methoxy group accelerates the reaction by a factor

of 10^3 to 10^4 the half-life for the solvolysis of α-(p-methoxyphenyl)-

ethyl bromide in ethanol at 25° is ten seconds to two minutes. The yield

of sulfone was measured at 12.95μ as α-(p-methoxyphenyl)ethyl ethyl

ether has significant absorption at 7.7μ and it was required to

measure possible small amounts of sulfone. A Lambert-Beer
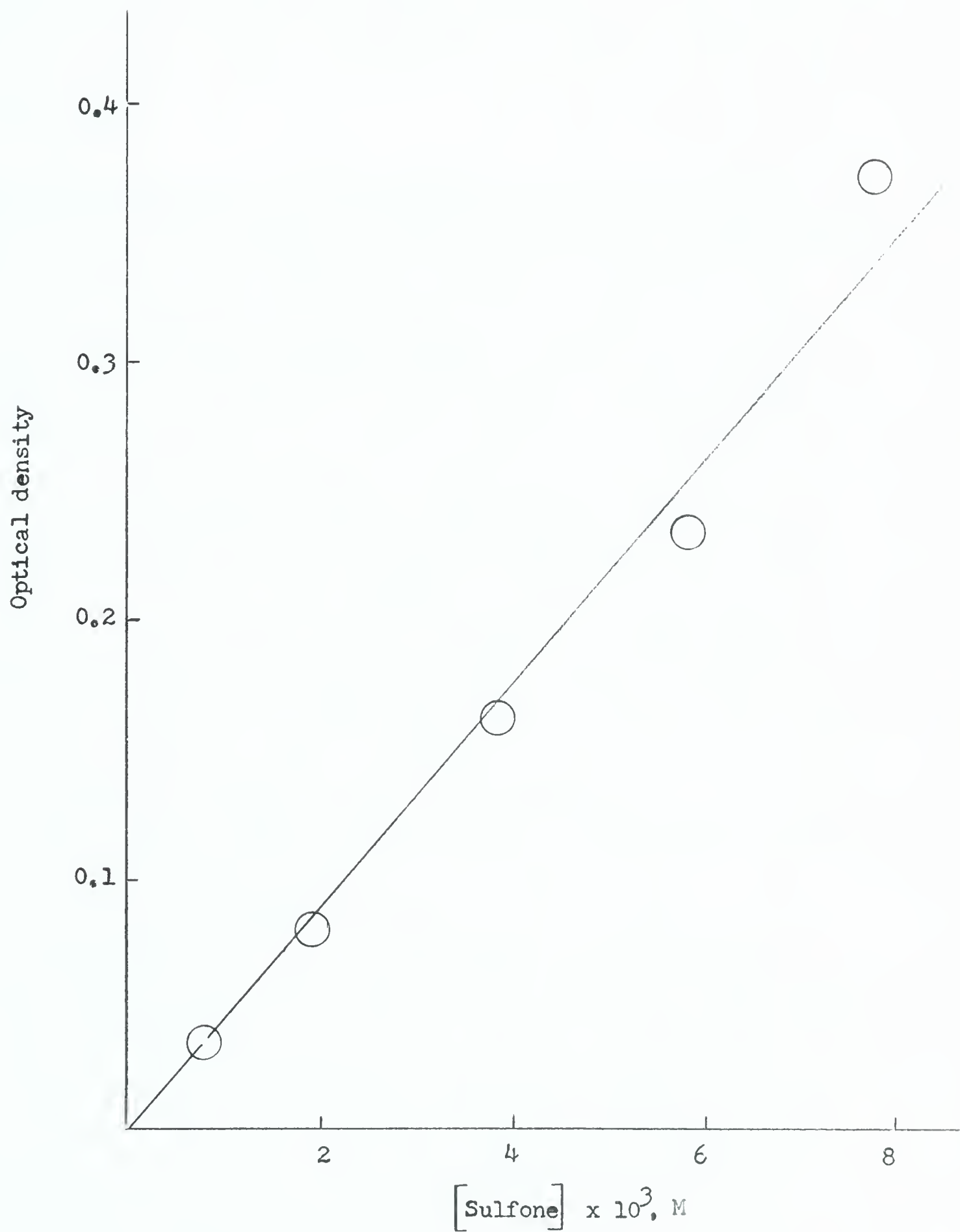
FIGURE XI

Lambert-Beer plot for α-(p-methoxyphenyl)ethyl 2,6-dimethylphenyl sulfone in bromoform at 12.95μ.

plot for the sulfone at 12.95μ is shown in Figure XI. In the above run the optical density at 12.95μ corresponded to a sulfone yield of less than 0.7 per cent.

Solvolysis and rearrangement of α-phenylethyl 2,6-dimethylbenzene-sulfinate in 60 per cent ethanol at 90° in the presence of sodium azide

The preparation of α-phenylethyl azide from α-phenylethyl chloride and sodium azide in aqueous methanol has been reported (39), but a major impurity was found to be also formed. It was presumably α-phenylethyl methyl ether and could be removed by chromatography on alumina. A more satisfactory method of preparation of α-phenylethyl azide consisted of the reaction of α-phenylethyl bromide with excess sodium azide in approximately 80 per cent acetone. A Lambert-Beer plot for this compound is shown in Figure XII. The same procedure was used to prepare α-(p-methoxyphenyl)ethyl azide from α-(p-methoxyphenyl)-ethyl chloride and a Lambert-Beer plot for this compound is also shown in Figure XII. Points from two different sets of measurements on azide obtained from two different preparations are distinguished.

A number of kinetic runs with α-phenylethyl 2,6-dimethyl-benzenesulfinate in 60 per cent ethanol in the presence of sodium azide were carried out and are reported in Table XXVIII. Except where stated the runs were carried out on the pure diastereomer. Good first-order rate constants were obtained by following the rate of disappearance of ester at 11.45μ. A sample rate is shown in Table XXIX. A plot of rate constant against sodium azide concentration (Figure XIII) is seen to be linear.

The products of the reaction in the presence of sodium azide were
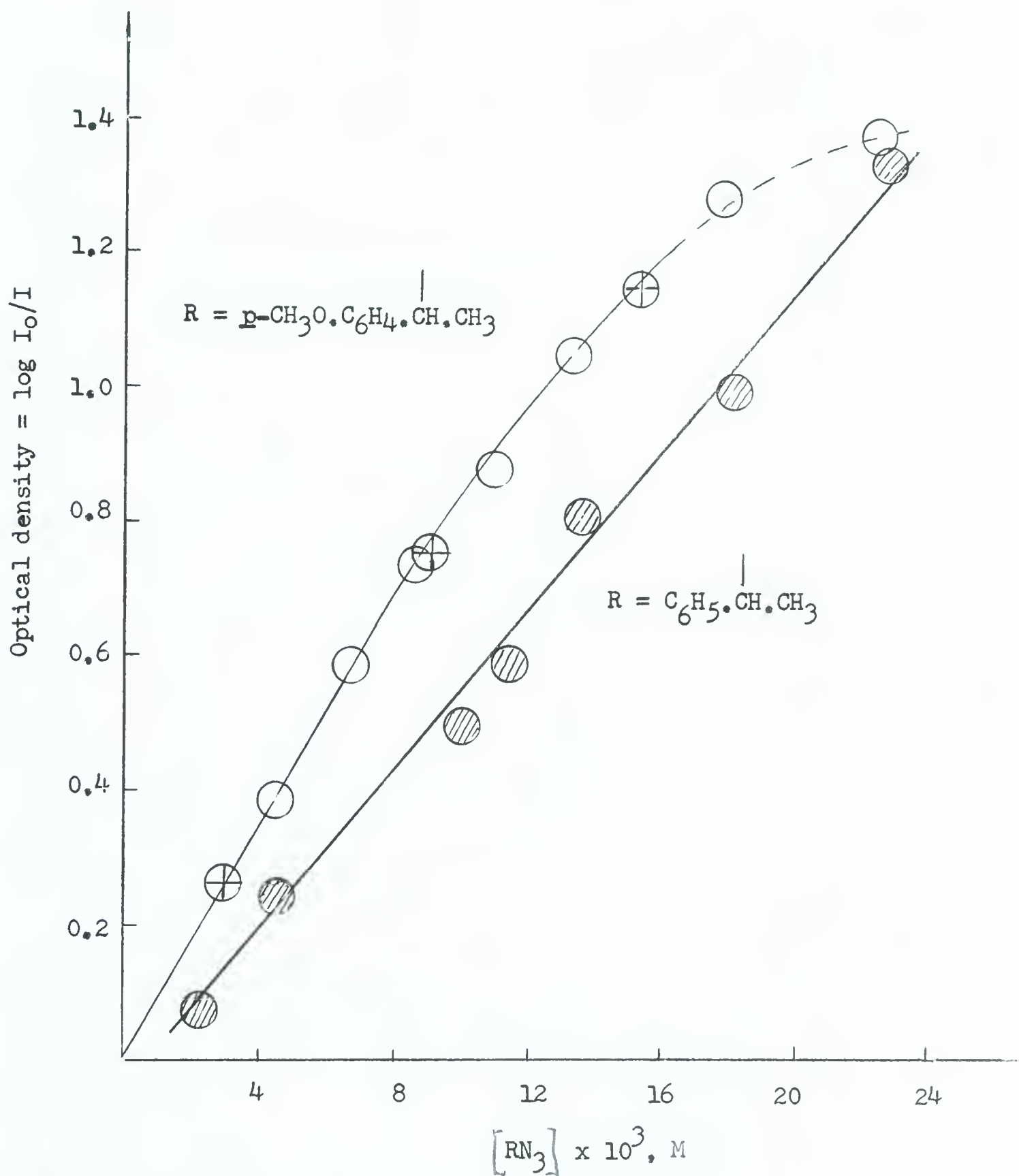
FIGURE XII

Lambert-Beer plots for α-phenylethyl azide and α-(p-methoxyphenyl)ethyl azide in CCl_4 at 4.80μ.

TABLE XXVIII

The solvolysis and rearrangement of α-phenylethyl 2,6-dimethylbenzenesulfinate in 60% ethanol at 90° in the presence of sodium azide.

Run	$[\text{Ester}]$	$[\text{2,6-Lutidine}]$	$[\text{NaN}_3]$	$k \times 10^5$, sec.$^{-1}$	Frear.
2-151	0.02238M	0.09649M	-	0.87 ± .03	0.111
2-203	.02378	.09649	0.04678M	0.99 ± .05	.110
2-154	.02206	.09649	.09513	1.17 ± .06	.087
2-204	.02214	.09696	.2054	1.54 ± .06	.055
2-243	.02247	.09747	.4597	2.52 ± .17	.039
2-209	.02511(a)	.09747	.4148	3.95 ± .37	.044
2-210	.02359(b)	.09747	.1086(c)	1.42 ± .21	.113

(a) 67% fast diastereomer.

(b) 65% fast diastereomer.

(c) Potassium thiocyanate.

TABLE XXIX

Rate of reaction of α-phenylethyl 2,6-dimethylbenzenesulfinate in 60%

ethanol at 90° in the presence of sodium azide (Run 2-243)

$[Ester]$ = 0.02247M, $[2,6\text{-Lutidine}]$ = 0.09747M, $[NaN_3]$ = 0.4597M

t(min.)	$D = \log I_0/I$	$\log D_0/D$	$k \times 10^5 \text{sec.}^{-1}$
0	0.7381	--	--
115	.6071	0.0849	2.82
252	.5015	.1679	2.55
424	.3799	.2886	2.60
605	.3123	.3737	2.37
1310	.1269	.7647	2.24
			Mean = 2.52 $\pm$ .17

also examined. The acid yield was measured titrimetrically and the

yields of sulfone and α-phenylethyl azide by the infrared method. The

results are reported in Table XXX. The measured yields of sulfone in

Tables XXVIII and XXX at similar azide ion concentrations are in good

agreement. First attempts at carrying out such an analysis gave non-

reproducible results and a number of control runs were carried out.

A solution of 2,6-dimethylbenzenesulfinic acid, sodium azide and

2,6-lutidine in 60 per cent ethanol was prepared. The initial titre was

in good agreement with that calcualted from the concentration of acid,

but successive titres showed a downward drift. This was attributed to

evaporation of hydrazoic acid when the flask was opened to withdraw a

sample and the remaining solution was placed in sealed tubes which were

heated at 90°. The acid titre was approximately constant over a period

TABLE XXX

Products from the reaction of α-phenylethyl 2,6-dimethylbenzenesulfinate in 60% ethanol at 90°

in the presence of sodium azide.

Run	[Ester]	[2,6-Lutidine]	[NaN$_3$]	% Yield of (a)			
				Sulfone	Acid	Azide (b)	Total
2-240	0.02179M	0.07798M	0.04849M	9.6 ± .6	61.2 ± 1.2	18.0 ± 0.8	88.8 ± 2.6
2-241	.02212	.07798	.1114	7.9 ± .5	41.4 ± 2.5	31.3 ± 3.1	80.6 ± 6.1
2-242	.02179	.07798	.2651	5.3 ± .3	13.1 ± 0.2	44.4 ± 5.4	62.8 ± 5.9
2-243	.02247	.09747	.4597	3.9 ± .3	7.5 ± 0.2	53.1 ± 9.0	64.5 ± 9.5

(a) Average of 2-4 measurements.

(b) α-Phenylethyl azide.
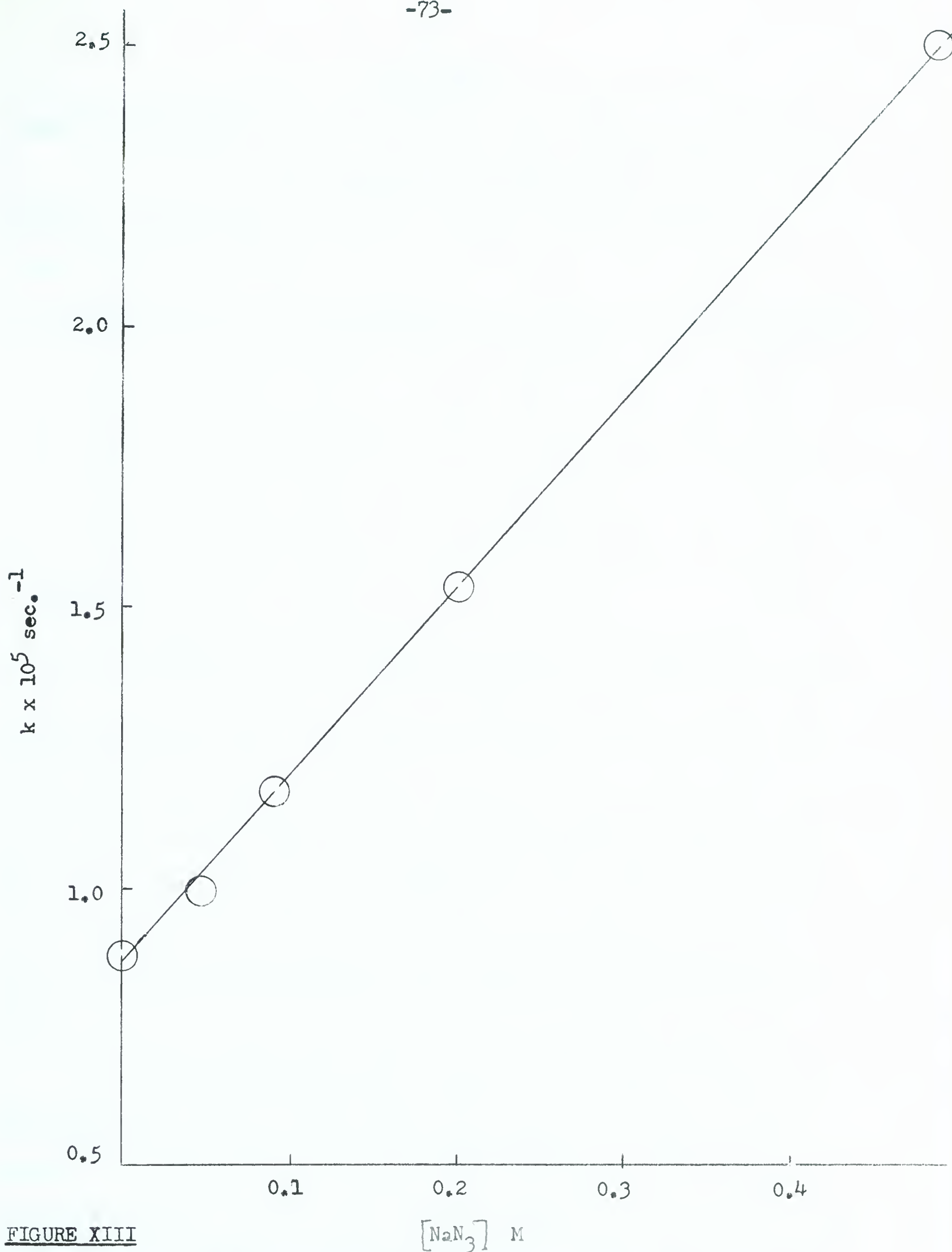
FIGURE XIII

$\left[\text{NaN}_3\right]$ M

Rate of reaction of α-phenylethyl 2,6-dimethylbenzenesulfinate in 60%

ethanol at 90° in the presence of sodium azide.

TABLE XXXI

Stability of 2,6-dimethylbenzenesulfinic acid in 60% ethanol at 90° in

in the presence of sodium azide

$\left[Acid\right]$ = 0.02733M, $\left[2,6\text{-Lutidine}\right]$ = 0.09747M, $\left[NaN_3\right]$ = 0.1817M

Calculated titre ‐ 3.715 ml.

Time	Titre (ml.)	Time	Titre (ml.)
(a)	3.705	1325 min.	3.386
(a)	3.630	8 days	3.810
(a)	3.552	8 days	3.745
(a)	3.504	10 days	3.811
3 min.	3.475	40 days	3.803
449 min.	3.445	40 days	3.806

(a) At room temperature. Specific times are for heating at 90°.

of 40 days (Table XXXI). The sharpness of the end point was poor due

to the buffering effect of hydrazoic acid (a similar effect was noted

in runs with a high concentration of 2,6-lutidine) but appeared not to

be shifted as the calculated and experimental titres were in agreement.

In obtaining the data of Table XXX care was taken not to leave the

solution exposed to the atmosphere for more than the minimum possible

time.

A solution of α-phenylethyl azide, sodium azide, 2,6-dimethyl-

benzenesulfinic acid and 2,6-lutidine in 60 per cent ethanol was pre-

pared. The same procedure as in a normal kinetic run at 90° was used.

As in the previous control the acid titre remained approximately constant

(Table XXXII). The measured optical density at 4.8μ was low for the

first two points. In subsequent measurements care was taken to pump the solution for the minimum time when removing pentane prior to preparation of the solution for infrared measurements. The optical density measurements were constant within experimental error over a period of eight days when this was done. One point was pumped overnight and over 90 per cent of the α-phenylethyl azide was lost. It thus appears that volatility of α-phenylethyl azide was the cause of the inconsistent result. After 40 days the optical density was apparently reduced (Table XXXII). However, the maximum reaction time in the runs reported in Table XXX was seven days and the azide was stable for that length of time. In obtaining the data of Table XXX care was taken to avoid loss of α-phenylethyl azide.

The total amount of the ester accounted for in Table XXX varies from 63-89 per cent, the discrepancy being more serious at higher azide concentrations. The control runs indicate that the error is not due to instability of the products or the method of analysis. A possible explanation is that sulfur-oxygen bond cleavage catalysed by azide ion occurs. The reaction of ethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol at 90° in the presence of sodium azide was accordingly examined. The results are reported in Table XXXIII. The reaction was followed by the disappearance of the ester band at 11.4μ and rate constants were calculated assuming the Lambert-Beer Law to hold. The reaction is apparently autocatalytic. No acid was formed in the reaction.

For an autocatalytic reaction of the type

$$A \longrightarrow B + \dots \, , \quad \text{rate} = k \left[A \right]\left[B \right]$$
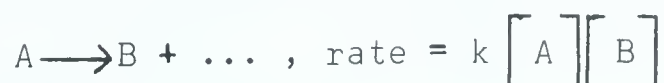
TABLE XXXII

Stability of 2,6-dimethylbenzenesulfinic acid and α-phenylethyl azide

in 60% ethanol at 90° in the presence of sodium azide

$[\text{Acid}]$ = 0.01682M, $[\text{2,6-Lutidine}]$ = 0.09747M, $[\text{RN}_3]$ = 0.01371M,

$[\text{NaN}_3]$ = 0.1011M, Calculated titre = 2.286 ml., calculated log I_0/I = 0.781

Time	Titre(ml.)	Pumping time	log I_0/I at 4.8μ
0	2.152	ca. 3 hrs.	0.6424
0	2.168	ca. 3 hrs.	0.5266
308 min.	2.106	minimum	0.8010
308 min.	2.110	minimum	0.7322
377 min.	2.112	overnight	0.0779
1212 min.	2.100	minimum	0.8547
8 days	2.150	minimum	0.7514
8 days	2.219	minimum	--
40 days	2.289	minimum	0.5721
40 days	2.348	minimum	0.5262

TABLE XXXIII

Reaction of ethyl 2,6-dimethylbenzenesulfinate in 60% ethanol at 90° in

the presence of sodium azide

$[\text{Ester}]$ = 0.02026M, $[\text{2,6-Lutidine}]$ = 0.09747M, $[\text{NaN}_3]$ = 0.3390M

Time (min.)	log I_0/I	log A_0/A(a)	k x 10^6,sec.$^{-1}$	log $(A_0-A)/A$
0	0.7817	--	--	--
1513	.7263	0.0320	0.81	$\bar{2}$.8785
2834	.6882	.0554	0.75	$\bar{1}$.1308
7051	.3994	.2917	1.59	$\bar{1}$.9810
10129	.1838	.6287	2.34	0.5123
13246	.0251	1.4934	4.32	1.4791

(a) A = optical density at 11.4μ.

$$kt(A_O + B_O) = 2.303 \log A_O B/B_O A \quad (40)$$

$$= 2.303 \log A_O/B_O + 2.303 \log B/A$$

If B_O is small, $B \doteq A_O - A$ and hence

$$2.303 \log (A_O - A)/A = kt(A_O + B_O) - 2.303 \log A_O/B_O$$

Thus a plot of $\log (A_O - A)/A$ should be linear in t. Because of the approximation made this will only hold when $(A_O - A)$ is large compared to B_O. Such a plot of the data from the above experiment (A = optical density) is shown in Figure XIV. It is seen to be linear.

A possible reaction under these conditions is a displacement of the sulfinate group from carbon by azide ion yielding ethyl azide. Accordingly ethyl azide was prepared from diethyl sulfate and sodium azide in water under basic conditions (41). The infrared spectrum showed a strong band at 2100 cm.$^{-1}$ but gas liquid chromatography showed the presence of two impurities. A trace of a compound having the same retention time as ethanol and about 20 per cent of an impurity with the same retention time as diethyl ether were apparent. A solution of this material (ca.0.002M) in 60 per cent ethanol containing 2,6-lutidine was prepared. The area of the peak from ethyl azide in this solution was approximately 15 times greater than a peak of the same retention time in the ethyl ester solution after more than 97 per cent reaction. No other products were visible due to the large amount of ethanol-water present. Thus less than 1 per cent ethyl azide is formed in the reaction of ethyl 2,6-dimethylbenzenesulfinate.

The nature of the reaction of the ethyl ester under these conditions is unknown. Attack of azide ion on carbon does not occur as ethyl azide is not a major product. Attack on sulfur, by azide ion or another
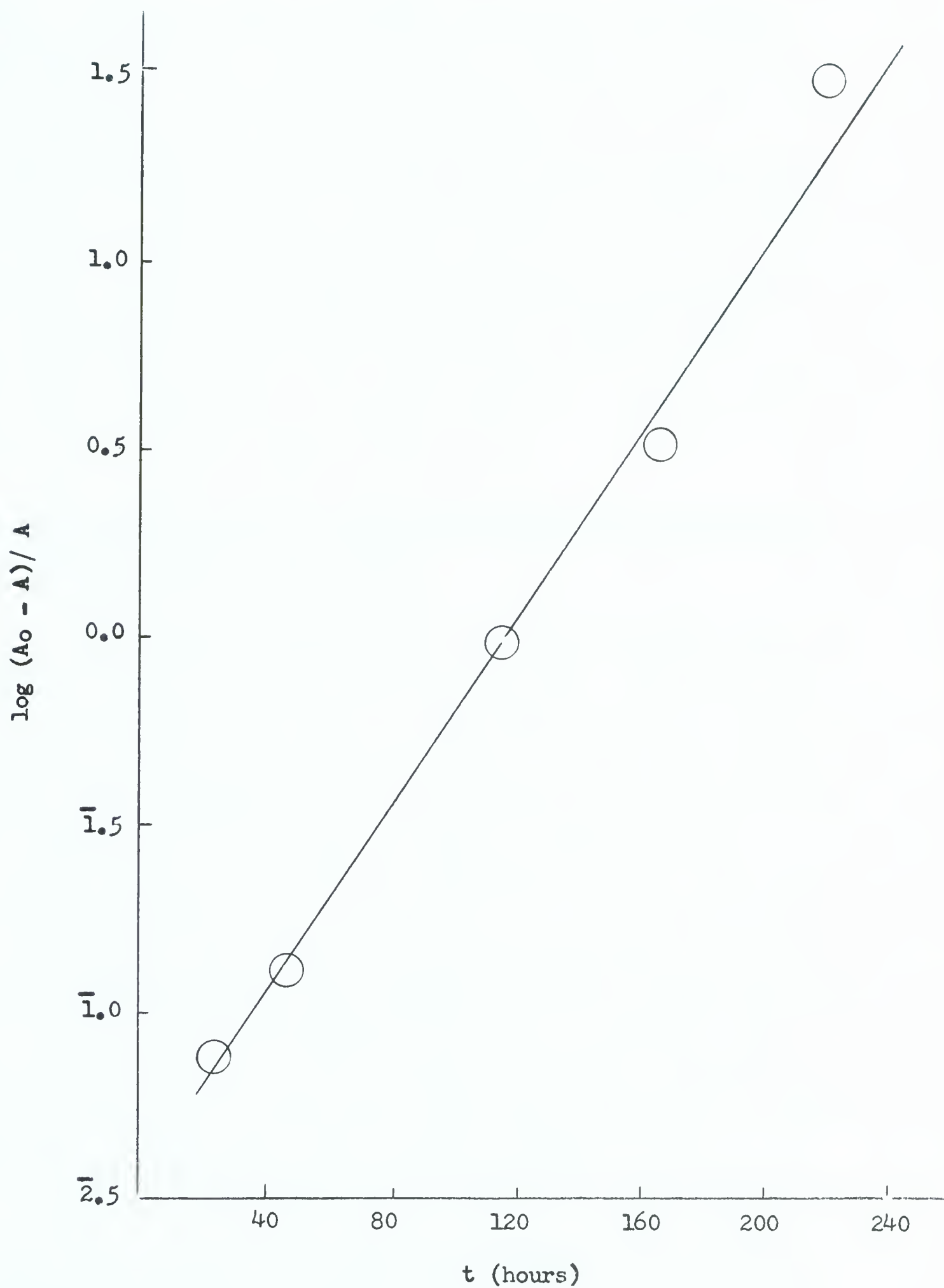
FIGURE XIV

The autocatalytic reaction of ethyl 2,6-dimethylbenzenesulfinate in
60% ethanol at 90° in the presence of sodium azide.

nucleophile, would be expected to lead to formation of 2,6-dimethyl-benzenesulfinic acid (2). Attack of azide ion followed by a Schmidt type of reaction is however another possibility.

The reaction appeard to be autocatalytic but the linear plot in Figure XIV may be coincidental, although the points represent 7-97 per cent reaction. It is possible that a similar reaction might compete with the solvolysis and rearrangement reactions of α-phenylethyl 2,6-dimethylbenzenesulfinate. This could account for the poor product analysis.

Solvolysis and rearrangement of α-(p-methoxyphenyl)ethyl 2,6-dimethyl-benzenesulfinate in 80 per cent ethanol

The effect of sodium azide on the solvolysis and rearrangement of this ester was studied in 80 per cent ethanol at 50°. The results are reported in Table XXXIV. The yields of azide and sulfone were measured at 4.8 and 7.65μ respectively. The reaction was followed by titrating the acid produced in the solvolysis reaction. At high azide ion concentrations the error in the rate constants is relatively large due to the small amount of acid formed and the buffering effect of sodium azide which made the end point less sharp than usual. A sample rate run is given in Table XXXV. The measured sulfone yield may be somewhat inaccurate as α-(p-methoxyphenyl)ethyl azide shows absorption at 7.8μ, overlapping the sulfone peak. Such errors are however unlikely to be large as the total product yields all lie in the range 94-106 per cent. It is clear from the data of Table XXXIV that sodium azide has a much greater effect on the yield of solvolysis products than it does on the yield of sulfone.

TABLE XXIV

The effect of sodium azide on the solvolysis and rearrangement of α-(p-methoxyphenyl)ethyl 2,6-dimethyl-

benzenesulfinate in 80% ethanol containing 0.09649 M 2,6-lutidine at 50°.

Run	[Ester]	[NaN₃]	$k \times 10^3$, sec.⁻¹	$F_{solv.}$	$F_{rear.}$	F_{azide} (a)	F_{total}
2-102	0.02242M	-	1.29 ± .04	0.68	0.315	-	0.995
2-106	.02124	0.07285M	1.51 ± .16	.46	.30	0.265	1.025
2-105	.01957	.1811	1.88 ± .17	.335	.27	.46	1.065
2-107	.02273	.3647	1.6 ± .3	.117	.23	.595	0.942

(a) Fraction of α-(p-methoxyphenyl)ethyl azide formed.

TABLE XXXV

The reaction of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate

in 80% ethanol at 50° in the presence of sodium azide (Run 2-105)

$\left[\text{Ester}\right]$ = 0.01957M, $\left[\text{2,6-Lutidine}\right]$ = 0.09649M, $\left[\text{NaN}_3\right]$ = 0.1811M,

calculated titre = 2.660 ml.

t(sec.)	Titre(ml.)	$\log(T_\infty - T_0)/(T_\infty - T)$	$k \times 10^3$,sec.$^{-1}$
0	0.194	--	--
180	0.427	0.1774	2.27
360	0.529	.2857	1.83
600	0.660	.4996	1.92
900	0.750	.7281	1.86
1260	0.778	.8334	1.52
269 min.	0.893		Mean = 1.88 $\pm$ .17
(∞)	0.885(a)		

(a) T_∞ = 0.889 ml. (33.5%).

Synthesis of optically active α-phenylethyl derivatives

The resolution of α-phenylethanol by way of the acid phthalate

and its brucine salt has been described by Kenyon (43). Following his

procedure samples of (+)- and (-)-α-phenylethanol of 77-90 per cent

optical purity (α_D + 17.03° to -19.52° (neat, l = 0.5)) were obtained.

All rotations reported are in 95 per cent ethanol unless otherwise

stated and at room temperature (27 $\pm$ 3°C). Preparation of 2,6-dimethyl-

benzenesulfinates by the usual procedure gave crystalline samples of

varying rotation and diastereomeric composition. The rotations and

compositions are listed in Table XXXVI. No pure diastereomer was

TABLE XXXVI

Properties of active α-phenylethyl 2,6-dimethylbenzenesulfinates

α_D^{ROH}(a)	%FD(b)	M.p. °C.	$[\alpha]_D^{ester}$(c)
+17.03°	64	43-47	-24.8°
-19.52	61	45-47	+14.8
-19.52	51	44-45.5	+11.5
-17.73	50	44-45	+1.0
-17.73	35	39-42	-23.6
+17.03	31	43-45	+78.5
-17.73	29	47-49	-21.3
-17.73	21	44-47	-37.5

(a) Rotation of alcohol used to prepare ester (neat, l = 0.5).

(b) Per cent fast diastereomer in ester.

(c) In ethanol.

isolated, but material rich in the slow diastereomer had the same sign of rotation as the alcohol used to prepare the ester and material rich in the fast diastereomer the opposite sign.

Active α-phenylethyl ethyl ether was prepared from the active alcohol by treatment with powdered potassium followed by ethyl bromide (3). α-Phenylethanol (α_D -19.522° (neat, l = 0.5), optical purity 89 per cent) gave (-)-α-phenylethyl ethyl ether, α_D -35.072° (neat, l = 0.5).   Kenyon (3) reported α_D -44.44° (neat, l = 0.5) for the optically pure ether.   The ether obtained is hence 79 per cent optically pure and since $[\alpha]_D$ (95% ethanol) was -90.4° the optically pure ether has $[\alpha]_D$ 115°.   This figure was used in calculating the optical purity of the ether obtained in the solvolysis reaction.

Optically active α-phenylethyl 2,6-dimethylphenyl sulfone was synthesised by the route shown in Figure VI except that other conditions were used for the conversion of α-phenylethanol to α-phenylethyl chloride. Treatment of α-phenylethanol (α_D -17.733° (neat, $\underline{l}$ = 0.5), optical purity 80%) with phosphorus oxychloride, pyridine, and pyridine hydrochloride in chloroform (44) gave (+)-α-phenylethyl chloride, α_D -41.802° (neat, $\underline{l}$ = 0.5). This reaction is known to form chloride of the opposite configuration to the starting alcohol and α_D (neat, $\underline{l}$ = 1) has been shown to lie between 109 and 126° for the optically pure chloride (44). Hence the chloride obtained was 66.5 to 76.8 per cent optically pure.

Treatment of the chloride with 2,6-dimethylthiophenol and sodium hydroxide in refluxing ethanol (98%) gave (-)-α-phenylethyl 2,6-dimethyl-phenyl sulfide, $\left[\alpha\right]_D$ -182°. Precipitation of sodium chloride appeared to be complete in less than one hour. In 100 per cent ethanol solvolysis of α-phenylethyl chloride has a rate constant of 5 x 10^{-6}sec.$^{-1}$ (45). From the activation parameters the rate constant at 76° can be calculated to be 8 x 10^{-5}sec.$^{-1}$, corresponding to a half-life of 2½ hours. Since the observed reaction is faster it must involve a displacement of chloride by thiophenolate ion and hence form sulfide opposite in con-figuration to the chloride. Due to the small difference between the observed rate and the calculated rate of solvolysis formation of some sulfide by an ionic mechanism is not excluded. This could give rise to partial racemisation.

In the above experiment the concentrations of sodium hydroxide and 2,6-dimethylthiophenol were approximately 1M and 0.5M respectively.

In ethanolic solution 2,6-dimethylthiophenolate ion would be present in approximately 0.5M concentration and total base in 1M concentration. α-Phenylethyl chloride in ethanol at 70° in the presence of 1M ethoxide reacts 5.5 times as fast as it does in the absence of ethoxide and the ethyl ether formed has predominantly inverted configuration (62). If all the rate increase is ascribed to a displacement of chloride by ethoxide it follows that 82 per cent of the product is formed by direct displacement. Thiophenolate ion is over 100 times as reactive towards n-butyl bromide in ethanol than is ethoxide ion (63,64). Since over 90 per cent yield of sulfide was isolated 2,6-dimethylthiophenolate must also be more nucleophilic than ethoxide and hence over 82 per cent of the reaction must have been a displacement. The sulfide thus has the same configuration as the alcohol of the same sign of rotation. Assuming that the sulfide has 82-100 per cent of the optical purity of the chloride, the sulfide can be calculated to be 55-77 per cent optically pure.

Oxidation of the above active sulfide with hydrogen peroxide gave α-phenylethyl 2,6-dimethylphenyl sulfone in 79 per cent yield, $[\alpha]_D$ -80.0°. A further crop corresponding to 5 per cent yield was also isolated, $[\alpha]_D$ -97.4°. Thus an 84 per cent yield of sulfone, $[\alpha]_D$ -81.1°, was obtained. Assuming the sulfone to have the same optical purity as the sulfide (55-77 per cent) $[\alpha]_D$ is 105-148° for the optically pure sulfone. The rotation of the first crop of sulfone was less than that of the second crop showing that the racemic sulfone is less soluble than the active sulfone. The same behaviour was noted during recrystallisation of the active sulfone. If it is assumed that the 16 per cent of the reaction unaccounted for gave optically pure sulfone which was not

isolated then the optical purity of the sulfone isolated could be as low as 46 per cent. Thus optically pure sulfone has $[\alpha]_D$ 105-177^0. Since no bonds are broken in the oxidation the sulfone must have the same configuration as the sulfide. Hence alcohol and sulfone of the same sign of rotation have the same configuration.

Recrystallisation of the major sulfone fraction from ethanol, recovering sulfone from the mother liquors, followed by three recrystallisations from ethanol in the usual way yielded α-phenylethyl 2,6-dimethylphenyl sulfone, $[\alpha]_D$ -127.6 $\pm$ .05^0, which did not change its rotation on further recrystallisation. It is probable that this sulfone is optically pure and in the calculation of the results from the product runs on optically active α-phenylethyl 2,6-dimethylbenzenesulfinate this was assumed.

Solvolysis and rearrangement of optically active α-phenylethyl 2,6-dimethylbenzenesulfinate in 60% ethanol at 90^0

The results of the experiments where the optically active products from the solvolysis of α-phenylethyl 2,6-dimethylbenzenesulfinate were isolated are given in Table XXXVII. The degree of stereospecificity was calculated by dividing the optical purity of the products by the optical purity of the alcohol used to prepare the ester. The ester used in these runs consisted of 36-49 per cent of the slow diastereomer. The method used to calculate the results is the only available one but is subject to error as it is not certain that the optical purity of the ester is the same as that of the alcohol used to prepare the ester. The sulfone is seen to be formed with almost complete retention of configuration and the solvolysis products with partial inversion.

TABLE XXXVII

The stereochemistry of the reactions of ⍺-phenylethyl 2,6-dimethylbenzene-

sulfinate in 60% ethanol at 90°

Run	[Ester]	[2,6-Lutidine]	$ArSO_2R$	Per cent retention in ROEt (a)	ROH (a)
2-162	0.03742M	0.09696M	98	36	34
2-170	.02934	.04848	95	30	0
2-231	.02643	.09747	97	--	27
2-232	.02677	.04874	--	38	32

(a) Inversion.

TABLE XXXVIII

Control run on optically active products from ⍺-phenylethyl 2,6-dimethyl-

benzenesulfinate in 60% ethanol at 90°

$$[\alpha]_D \text{ (EtOH)}$$

Compound	Initial	After heating	After reisolation
ROEt	-90.4	-83.5	-78.2
ROH	+33.7	+27.8	+28.2
$ArSO_2R$	-72.5	-65.9	-64.0

In a control run a solution of the three products of known optical

purity was heated at 90° for ten days (12 half-lives for reaction of the

slow diastereomer) in 60 per cent ethanol in the presence of 2,6-lutidine

and the compounds isolated. These results are reported in Table XXXVIII.

The measured rotations were somewhat lower than at the start of the

experiment. That this difference was not due to the presence of solvent

was shown by reisolating the compounds and measuring the rotations after

solvent was definitely removed. The values were within experimental
error of those found previously (Table XXXVIII). The values of the
optical purities in Table XXXVII can therefore be taken to be minimal.
No explanation is advanced for the discrepancy in the stereochemistry
of the alcohol isolated in Run 2-170.

Polarimetric rate constants could be obtained from ester samples
having a relatively high rotation. The rate constants are reported in
Table XXXIX and a sample rate given in Table XL. In 60 per cent
ethanol the polarimetric rate constant is within experimental error of
the titrimetric and infrared rate constants, the mean value of the
polarimetric rate constants being $(1.02 \pm .18) \times 10^{-5} sec.^{-1}$.

Interconversion of diastereomers during solvolysis

The pure diastereomer of α-phenylethyl 2,6-dimethylbenzene-
sulfinate (0.02500M) was allowed to react in 60 per cent ethanol
containing 2,6-lutidine (0.09696M) at 90° for 21.5 hours (approximately
one half-life) and the product mixture isolated. The nuclear magnetic
resonance spectrum showed three peaks in the region 7.5-7.7τ, assigned
to the aromatic methyl groups. The major peak was at 7.59τ and was
due to the starting diastereomer. Two smaller peaks were present at
7.51 and 7.69τ . The latter can be assigned to the sulfone which is
known to be formed and a peak at 7.51τ is present in the spectrum of
the diastereomeric ester. However, 2,6-lutidine also has a peak at 7.5τ.
The mixture was dissolved in pentane, washed with hydrochloric acid
and reisolated. The spectrum was unchanged. The peak at 7.51τ can
therefore be assigned to the diastereomeric α-phenylethyl 2,6-dimethyl-
benzenesulfinate. The relative area of the peaks at 7.51 and 7.69τ was
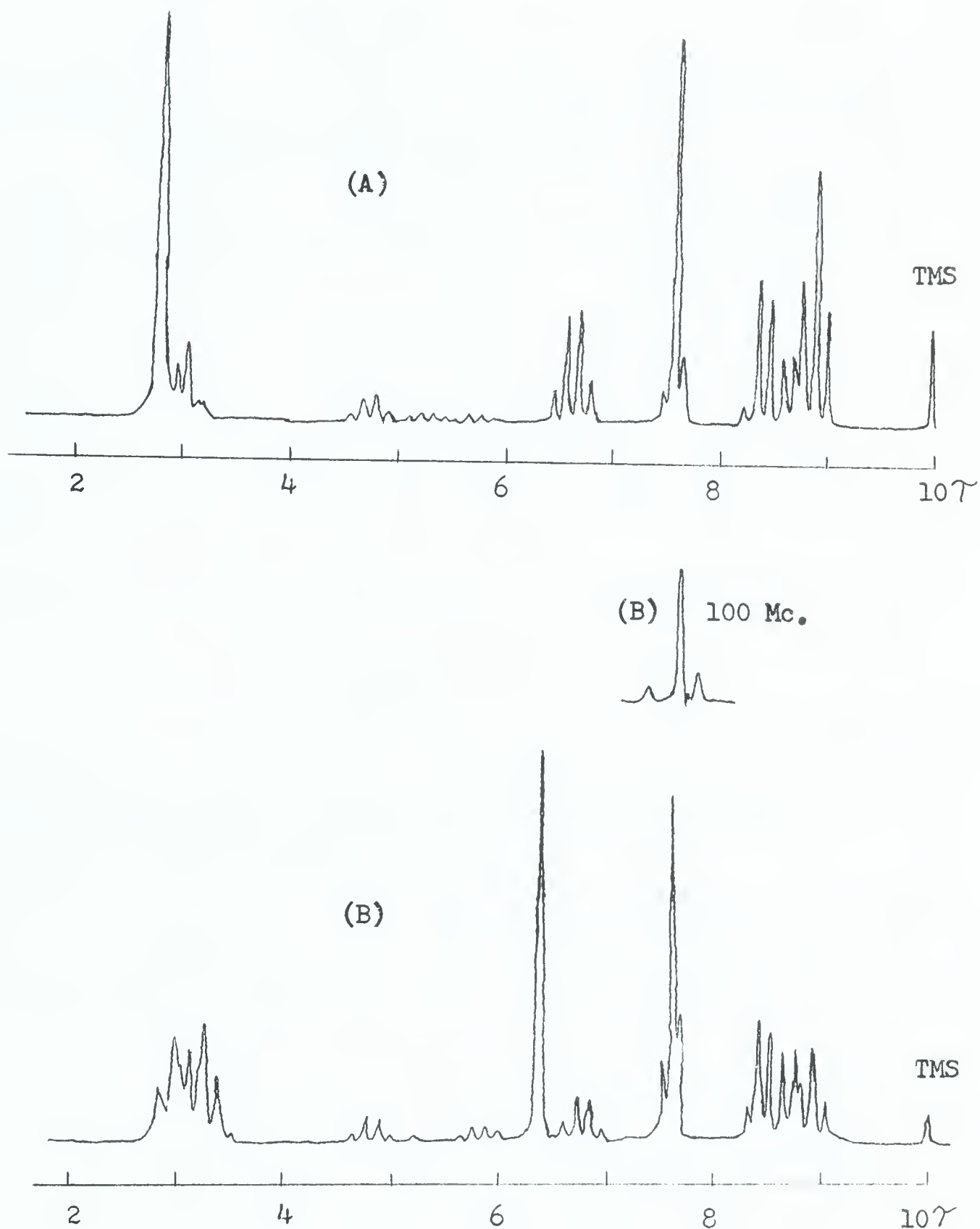
FIGURE XV

N.m.r. spectra (CS$_2$) of α-phenylethyl 2,6-dimethylbenzenesulfinate after 50% reaction in 60% ethanol at 90° (A) and of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate after 50% reaction in ethanol at 70° (B).

TABLE XXXIX

Polarimetric rate of reaction of α-phenylethyl 2,6-dimethylbenzene-

sulfinate in 60% ethanol at 90°

Run	[Ester]	$[\alpha]_D^o$	[NaOAc]	$k \times 10^5, \text{sec.}^{-1}$
1-154	0.02899M	+18.1(a)	.1010M	$1.29 \pm .41$
1-166	.02912	-72.4	.1025	$0.75 \pm .12$
2.237	.03235	+78.5	.09647(b)	$1.01 \pm .23$

(a)   4 dm. Polarimeter tube used.   Other runs were carried out using a 1
dm. tube.

(b)   2,6-Lutidine

TABLE XL

Polarimetric rate for α-phenylethyl 2,6-dimethylbenzenesulfinate

(31% fast diastereomer) in 60% ethanol at 90° (Run 2-237)

[Ester] = 0.03235M,   [2,6-Lutidine] = 0.09674M

t(min.)	α_D^o (l = 1 dm.)	$\log\ (\alpha_o - \alpha_\infty)/(\alpha - \alpha_\infty)$	$k \times 10^5, \text{sec.}^{-1}$
0	0.587	--	--
153	.521	0.0565	1.42
237	.509	.0676	1.09
340	.472	.1038	1.17
513	.499	.0771	0.58
741	.436	.1421	0.74
1381	.302	.3250	.090
1772	.206	.5291	1.14
9 days (∞)	.046	--	---

Mean = $1.01 \pm .23$

estimated gravimetrically as 0.38:1. The spectrum is shown in Figure XV.

Since the diastereomer formed in the reaction reacts faster than the

starting isomer this is a minimum estimate of the amount of isomerisation

occurring under these conditions. Since from other evidence 6 per cent

sulfone is formed in the time allowed, 2-3 per cent of the diastereomer

is present at the end of one half-life of the reaction. The n.m.r.

spectrum after ten half-lives showed no peaks in the 7.5τ region.

For the reaction scheme

$$A_1 \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} A_2$$

$$A_1 \xrightarrow{k_{13}} A_3 \xleftarrow{k_{23}} A_2$$

$$A_3$$
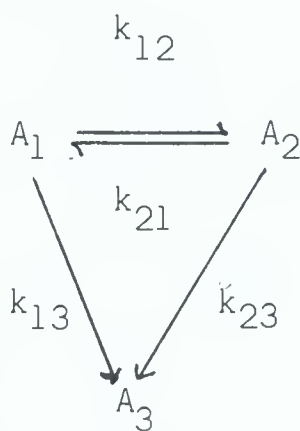
$$A_2/A_1^0 = \frac{(k_{12} + k_{13} + \lambda_2)(k_{12} + k_{13} + \lambda_3)}{k_{21}(\lambda_3 - \lambda_2)} (e^{-\lambda_3 t} - e^{-\lambda_2 t})$$

where $\lambda_2 = \frac{1}{2}(k_{12} + k_{13} + k_{21} + k_{23} + \sqrt{(k_{12} + k_{13} + k_{23} + k_{21})^2 - 4(k_{12}k_{23} + k_{13}k_{23} + k_{13}k_{21})}$

and

$$\lambda_3 = \frac{1}{2}(k_{12} + k_{13} + k_{21} + k_{23} - \sqrt{(k_{12} + k_{13} + k_{23} + k_{21})^2 - 4(k_{12}k_{23} + k_{13}k_{23} + k_{13}k_{21})}$$

This expression is equivalent to that reported by Lewis and Johnson

(75) for the same scheme except that a number of misprints are present

in their paper. Another expression, equivalent to the above, is

$$A_2/A_1^0 = \frac{k_{12}}{\lambda_2 - \lambda_3} (e^{-\lambda_3 t} - e^{-\lambda_2 t})$$

In the above scheme, if A_1 is the slow diastereomer and A_2 the fast diastereomer, $k_{13} = 1 \times 10^{-5}$ sec.$^{-1}$ and $k_{23} = 1.6 \times 10^{-5}$ sec.$^{-1}$. Assuming that $k_{12} \approx k_{21}$, as will be at least approximately true, the best fit to the experimental results is given when k_{12} is approximately 1×10^{-6} sec.$^{-1}$. Then $A_2/A_1^0 = 0.026$ after 20 hours reaction time.

The pure diastereomer of α-(p-methoxyphenyl)ethyl 2,6-dimethyl-benzenesulfinate (0.01687 M) and 2,6-lutidine were allowed to react in ethanol at 70° for 22 minutes (ca. one half-life). The nuclear magnetic resonance spectrum of the product mixture isolated was taken at 100 Mc. as the three aromatic methyl peaks at 7.59, 7.67 and 7.71 $\mathcal{T}$ were not well enough resolved at 60 Mc. to allow of reasonably accurate measurement. The peaks are assigned to the fast diastereomer, slow diastereomer and sulfone, respectively. The ratio of fast diastereomer to sulfone was 0.50. The spectrum is shown in Figure XV.

The experiment was repeated in the presence of 0.2240 M tetra-butylammonium azide for 20 minutes at 70°. The ratio of fast diaster-eomer to sulfone was 0.54. Titrimetric and infrared measurements indicated that the yields of acid, sulfone and α-(p-methoxyphenyl)-ethyl azide were 28.2, 13.4, and 14.2 per cent respectively. Therefore the fractions of solvolysis, rearrangement and azide formation were 0.51, 0.24 and 0.25 respectively. When these are compared with 0.71, 0.29 and 0.00 as obtained in the absence of azide ion (see Tables XXIII and XXV) it is seen that the yield of solvolysis products is more sensitive to the presence of azide ion than is the yield of sulfone. This is the same as observed in 80 per cent ethanol where the amount of α-(p-methoxyphenyl)ethyl azide formed is about twice as great for the

same concentration of azide ion (Table XXXIV).

In the kinetic scheme above it was assumed that $k_{13} = 6 \times 10^{-4} \text{sec.}^{-1}$ and $k_{23} = 9 \times 10^{-4} \text{sec.}^{-1}$. If $k_{12} = k_{21} = 2 \times 10^{-4} \text{sec.}^{-1}$ then $A_2/A_1^0 = 0.074$. If $k_{12} = 3 \times 10^{-4} \text{sec.}^{-1}$ and $k_{21} = 10 \times 10^{-4} \text{sec.}^{-1}$ then $A_2/A_1^0 = 0.072$ after 20 minutes reaction time. Since 14 per cent sulfone is formed in the first half-life and the ratio fast diastereomer:sulfone is 0.50, the experimental value of A_2/A_1^0 is 0.07. The values of k_{12} and k_{21} given above are, of course, not the only values which will give an A_2/A_1^0 ratio in agreement with the experimental results. Since we are solving one equation in two unknowns, k_{12} and k_{21}, there are an infinite number of solutions. However, k_{21} cannot be negative and this requires k_{12} to be greater than $1.5 \times 10^{-4} \text{sec.}^{-1}$.

DISCUSSION

It has been concluded in Chapter I that both the solvolysis and rearrangement reactions of both esters are ionic in nature. Sulfone formation could occur intramolecularly by ion pair return, inter-molecularly by the combination of free carbonium and sulfinate ions or by a combination of these two pathways. There are a number of pieces of evidence which point to the first route as being the most important mechanism of sulfone formation in the examples studied.

Firstly there was no apparent upward drift in the fraction of sulfone formed from α-phenylethyl 2,6-dimethylbenzenesulfinate as the reaction proceeded (Tables XXI and XXII). If the sulfone was formed by an intermolecular mechanism it would be expected that more sulfone would be formed as the concentration of sulfinate ion in the solution increased. For both esters the reaction was conducted in the presence of added 2,6-dimethylbenzenesulfinate ion (2,6-dimethylbenzenesulfinic acid + excess base) which should increase the yield of sulfone if an inter-molecular mode of formation is of importance. No such increase was apparent for α-phenylethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol (Table XVIII) or for α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzene-sulfinate in ethanol (Table XXV) and in 60 per cent ethanol (Table XXVII).

The solvolysis of α-phenylethyl bromide in 60 per cent ethanol and of α-(p-methoxyphenyl)ethyl bromide in ethanol, both in the presence of 2,6-dimethylbenzenesulfinate ion, gives rise to negligibly small amounts of the corresponding sulfones. To the extent that the ionisa-tion of α-phenylethyl bromide and of α-(p-methoxyphenyl)ethyl bromide

is analogous to the ionisation of the corresponding 2,6-dimethylbenzene-sulfinates the above results are indicative of the relative unimportance of the intermolecular pathway to sulfone in the reaction of the sulfinate esters.

Thus it appears that under the conditions studied the major part of the rearrangement reaction is intramolecular and intermolecular rearrangement is unimportant. Sulfone formation in these cases is an example of ion pair return with rearrangement of the anionic portion of the molecule. It may be compared to randomisation of the carboxylate oxygen atoms in benzoates (15) and to the thionbenzoate-thiolbenzoate rearrangement (17). Both these reactions however involve a 1,3 shift of the cationic portion of the molecule whereas the sulfinate-sulfone rearrangement involves a 1,2 shift.

The question of whether free ions are involved in the solvolysis reactions cannot be unequivocally answered at the present time. When common ion rate depression is observed return from free ions must occur but the converse is not necessarily true. If free ions are formed but react exclusively to give products or exclusively to give solvent separated ion pairs then common ion rate depression will not be observed (11). The fact that no common ion rate depression has been observed in any of the cases studied does not therefore rule out the formation of solvolysis products from free ions.

In the reaction of α-phenylethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol there is one piece of evidence that suggests that free ions are unimportant in the solvolysis. Both of the solvoly-sis products isolated from the reaction of optically ester are about 30%

inverted (Table XXXVII). Solvolysis products from the free carbonium ion should be completely racemic as the free carbonium ion has of necessity lost all asymmetry. Partial or complete racemisation of a solvent separated ion pair might also be expected. Even an ion pair of completely retained configuration might not be expected to give completely inverted solvolysis products as solvent attack on the same side of the carbonium ion as the leaving group could conceivably occur. Relevant to this discussion is the work of Goering on optically active p-chlorobenzhydryl p-nitrobenzoate (15,16). In aqueous acetone about 40 per cent of ion pair return leads to racemisation of the ester (15) and the intimate ion pair was shown to be unracemised (16). It follows that the solvent separated ion pair must be partially racemised. The fairly high stereospecificity of the solvolysis of α-phenylethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol indicates that ion pairs are probably the most important intermediates.

Sulfone formation could occur by internal return from an intimate ion pair, by external ion pair return from a solvent separated ion pair or by a combination of the two pathways. The results of the rearrangement of optically active α-phenylethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol have a bearing on this. The sulfone isolated from the reaction was over 95 per cent retained in configuration (Table XXXVII). By analogy with the results of Goering this is indicative of sulfone formation by internal return from an intimate ion pair.

It is not clear from the results of Tables XXVIII and XXX whether α-phenylethyl azide formation proceeds by way of a direct displacement of sulfinate ion by azide ion or by reaction of azide ion

with a carbonium ion species. If the products derived from α-phenyl-
ethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol in the

presence of azide ion were accurately known it might be possible to

distinguish these two possibilities as is done below for the substituted

ester. The effects of azide ion on the solvolysis and rearrangement

reactions appear to be qualitatively similar. This is consistent with

a direct displacement or with interception of a similar intermediate

(or intermediates) by azide ion.

The following mechanism for the solvolysis and rearrangement of
α-phenylethyl 2,6-dimethylbenzenesulfinate in 60 per cent ethanol is

consistent with the observed facts.

$$Ar \overset{\displaystyle\uparrow\text{O}}{\underset{\displaystyle\downarrow\text{O}}{-\ \text{S}\ -}} R$$

$$Ar.SO.OR \rightleftharpoons ArSO_2^-\ R^+ \rightleftharpoons ArSO_2^-//R^+ ----\rightarrow ArSO_2^- + R^+$$

Solvolysis products
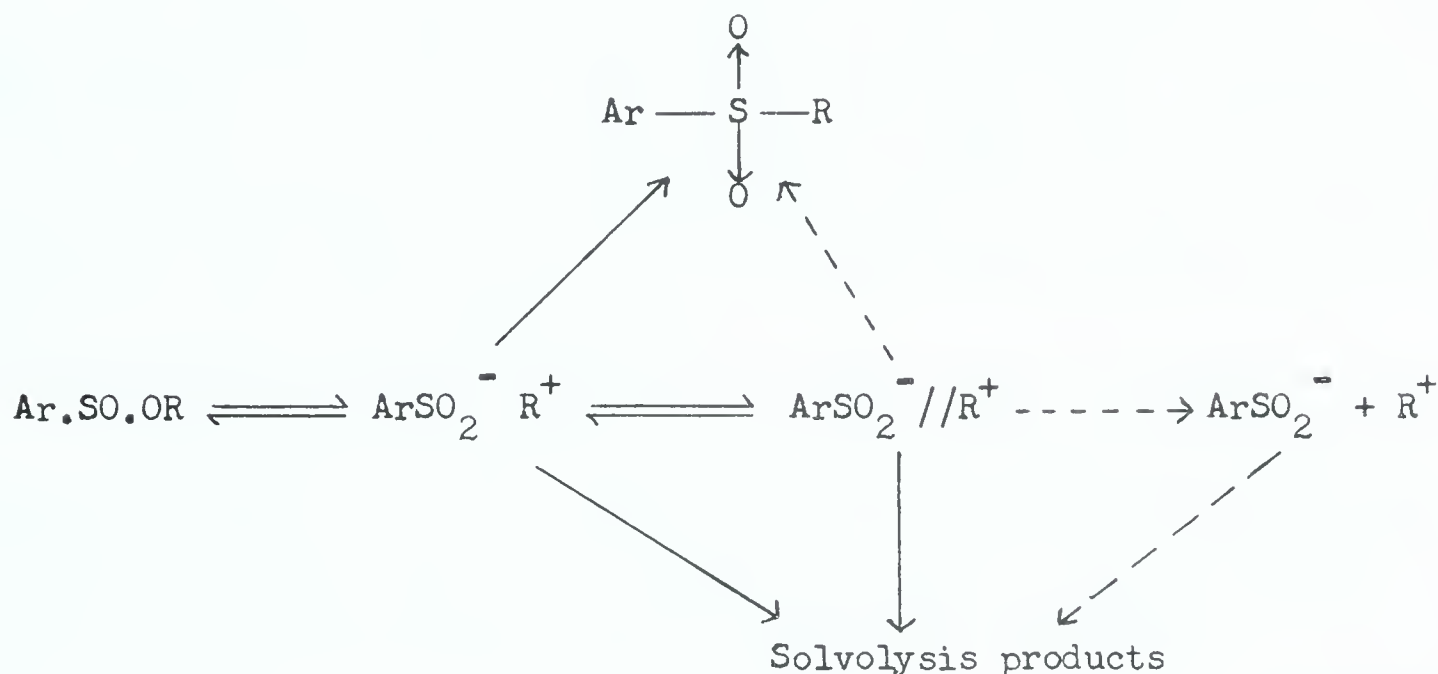
The reactions indicated by solid arrows are considered most likely but

those shown by dotted arrows cannot be definitely ruled out.

The details of the mechanism of the solvolysis and rearrangement

of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate are not so

clear as we have no data on the stereochemistry of the reaction. The

results of the experiments carried out on the effect of sodium azide on the reaction in 80 per cent ethanol are however informative. The yield of solvolysis products is reduced by sodium azide to a much greater extent than is the yield of sulfone. Since the solvolysis and rearrangement reactions show such different sensitivities to the presence of sodium azide it appears that the major routes to sulfone and solvolysis products in this medium involve different intermediates. That α-(p-methoxyphenyl)ethyl azide formation is the result of reaction of a carbonium ion species is shown by two facts. Displacement of the sulfinate group in the ester by azide ion would lead to equal reduction of the sulfone and solvolysis yields. However, this is not observed. Also, the increase in rate in the presence of 0.36M sodium azide is approximately 50 per cent. If all the rate increase were attributed to a displacement reaction the expected yield of α-(p-methoxyphenyl)ethyl azide from this source would be about 33 per cent whereas the observed yield is 60 per cent (Table XXXIV).

Since the product distribution is very similar in 60 per cent, 80 per cent and 100 per cent ethanol it is unlikely that any important mechanistic change occurs on changing the solvent. The most likely explanation of the results is shown below.

$$Ar.SO.OR \rightleftharpoons Ar.SO_2^- R^+ \rightleftharpoons Ar.SO_2^- // R^+$$
$$\downarrow \qquad\qquad\qquad \downarrow$$
$$Sulfone \qquad\qquad Solvolysis\ products$$
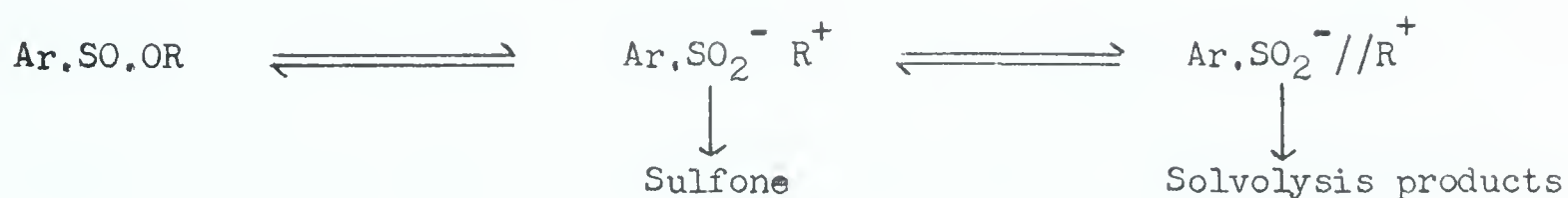
As stated above the intermediacy of free ions in the solvolysis reaction cannot be ruled out. Since no stereochemical evidence is

available the following mechanism is a definite possibility.

$$\text{Ar.SO.OR} \quad \rightleftharpoons \quad \text{Ar.SO}_2^-/\text{R}^+ \quad \longrightarrow \quad \text{Ar.SO}_2^- + \text{R}^+$$

$$\downarrow \qquad\qquad\qquad\qquad\qquad \downarrow$$

Sulfone   Solvolysis products
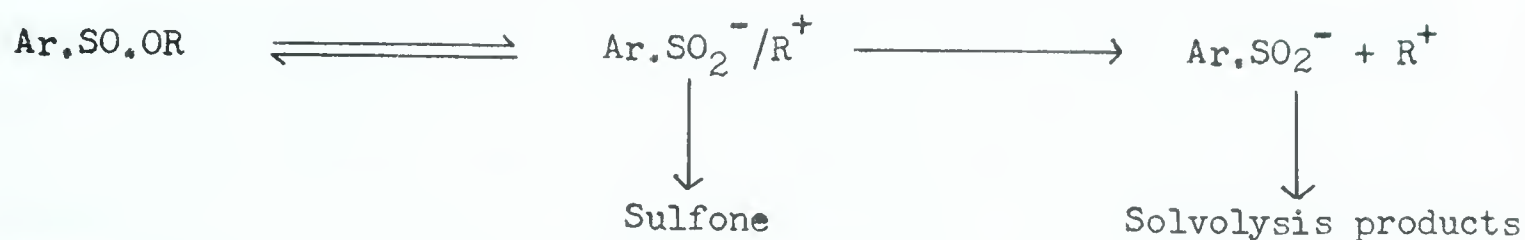
$\text{Ar.SO}_2^-/\text{R}^+$ = an ion pair of undefined type.

In the second mechanism two ion pairs could also be involved, both giving sulfone but only one giving solvolysis products.

The formation of the diastereomeric sulfinate esters during solvolysis could proceed by four different mechanisms. These are vibrational inversion about sulfur analogous to the rapid inversion in amines, a cyclic four-membered rearrangement, sulfur-oxygen bond cleavage or by ionisation. There is no evidence for the formation of any of the expected products from sulfur-oxygen bond cleavage under conditions where the interconversion of diastereomers occurs and it is difficult to conceive of a mechanism for the interconversion of diastereomers involving such cleavage which would not give rise to products derived from the solvent. It would not be expected that the presence of a methoxy substituent would greatly affect the rate of the first three processes. In fact the interconversion of diastereomers is approximately as sensitive to the presence of a methoxy substituent as are the solvolysis and rearrangement reactions, i.e., the ratio of diastereomer and sulfone formation is approximately the same for both esters. This is consistent with diastereomer formation by ionisation but inconsistent with the other three possible explanations.

Since inversion in the sulfinate ion would not be expected to be significantly easier than in the esters the most likely mechanism of

interconversion involves ionisation followed by the creation of a new

carbon-oxygen bond. Another possible explanation is partial inversion

of the carbonium portion ion of the molecule (i.e., racemisation) with

reformation of the original carbon-oxygen bond. In the latter case the

oxygen atoms of the sulfinate ion must certainly become equivalent and

formation of a new carbon-oxygen bond occur. Formation of a new carbon-

oxygen bond to an inverted carbonium ion would however give rise to the

starting diastereomer as both portions of the molecule have been

inverted. The possibilities are illustrated below where (A) and (B)

designate the two diastereomers.

$$
\begin{array}{c}
OR \\
| \\
O \leftarrow \overset{}{S}.Ar \\
(A)
\end{array}
$$

$$
\begin{array}{ccccc}
\overset{O}{\overset{\uparrow}{Ar.S}} \!-\! OR & \rightleftharpoons & Ar.SO_2^{-} \; R^{+} & \rightleftharpoons & R^{+} \; {}^{-}O_2S.Ar \\
(A) & & & & \\
& & \updownarrow & & \updownarrow \\
& & \begin{array}{c} OR \\ | \\ Ar.S\!\rightarrow\!O \end{array} & & \begin{array}{c} O \\ \uparrow \\ RO\!-\!S.Ar \end{array} \\
& & (B) & & (B)
\end{array}
$$
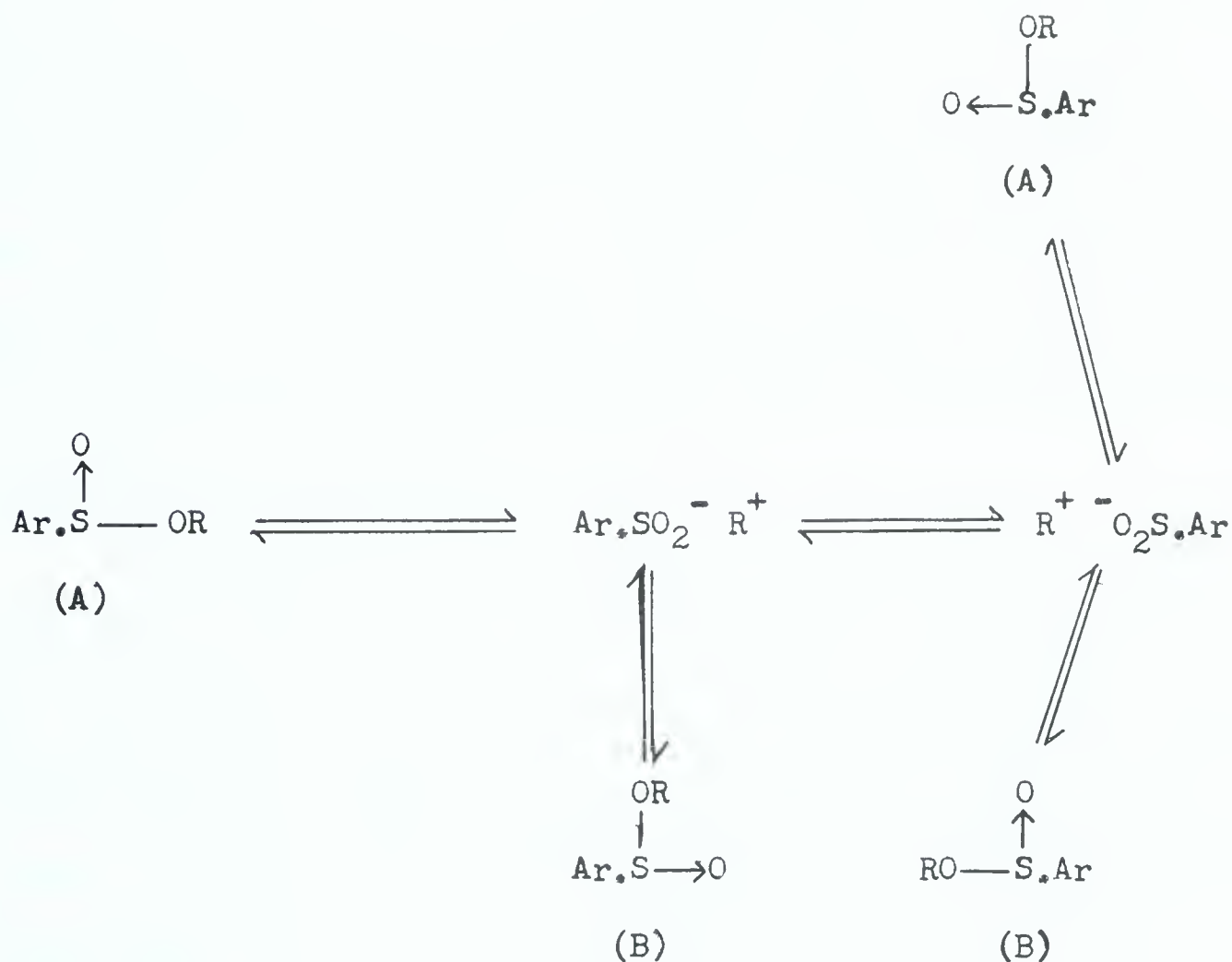
It is reasonable that formation of a new carbon-oxygen bond would

occur under conditions where the diastereomers are interconverted. This

could be verified experimentally by an ^{18}O labelling experiment which has not yet been carried out, however. The interconversion of dias- tereomers by racemisation of the carbonium ion is experimentally demonstrable in theory but would be very difficult in practice. The experiment would involve preparation of an optically active pure diastereomer, partial reaction, separation of the diastereomers and determination of their stereochemistry.

In the case of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzene- sulfinate in ethanol the interconversion of diastereomers is unaffected, or affected to the same small extent as sulfone formation, by the presence of azide ion. Since sulfone formation has been shown to be intramolecular diastereomer formation must also be intramolecular. In this case at least diastereomer formation by ion pair return occurs. Both possible mechanism involve formation of a new carbon-oxygen bond and hence the isomerisation is directly comparable to the randomisation of the carboxylate oxygens in benzoates (15) and the thionbenzoate- thiolbenzoate rearrangement (17).

Since the ratio of isomerisation to rearrangement is about the same for both esters it is reasonable that both reactions might involve the same intermediate, the product depending on the relative amounts of carbon-oxygen and carbon-sulfur bond formation. In the reaction of trityl perchlorate, tetrabutylammonium azide and tetrabutylammonium 2-methylbenzenesulfinate in acetonitrile about equal amounts of trityl 2-methylbenzenesulfinate and trityl 2-methylphenyl sulfone are estimated to be formed initially (18). This suggests that each oxygen in the sulfinate ion has about half as much chance of combining with the trityl

carbonium ion as the sulfur atom does. If the trityl carbonium ion in acetonitrile is a reasonable model for the α-arylethyl carbonium ion in hydroxylic media it would be expected that half as much isomerisation as rearrangement would occur, as is in fact observed. However if the oxygen atoms of a sulfinate ion in an ion pair are not equivalent this prediction would not necessarily hold.

The reaction schemes in Figures XVI and XVII are extensions of those proposed earlier for the solvolysis and rearrangement reactions, incorporating diastereomer formation from the same intermediates which give sulfone. It should however be borne in mind that as already stated other possibilities exist for the solvolysis and rearrangement reactions. The three schemes are consistent with the results but are not necessarily the only routes possible to the various products. Scheme A in Figure XVII is the minimum required to accommodate the results. The formation of diastereomeric α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate has been shown not to involve free ions, but any other ionic inter-mediates may be involved in the isomerisation reaction.

Ion pair return to give the starting diastereomer without racemisation would not be detectable under any circumstances. If the two oxygen atoms in the sulfinate ion of an ion pair were equivalent then return on each oxygen would be equally probable. If this is true and the interconversion of diastereomers occurs without racemisation of the carbonium ion it follows that the total amount of ion pair return to ester would be twice the ion pair return to diastereomeric ester and approximately equal to the amount of ion pair return to give sulfone, since the extent of isomerisation is about half that of rearrangement for

FIGURE XVI

The solvolysis and rearrangements of α-phenylethyl
2,6-dimethylbenzenesulfinate
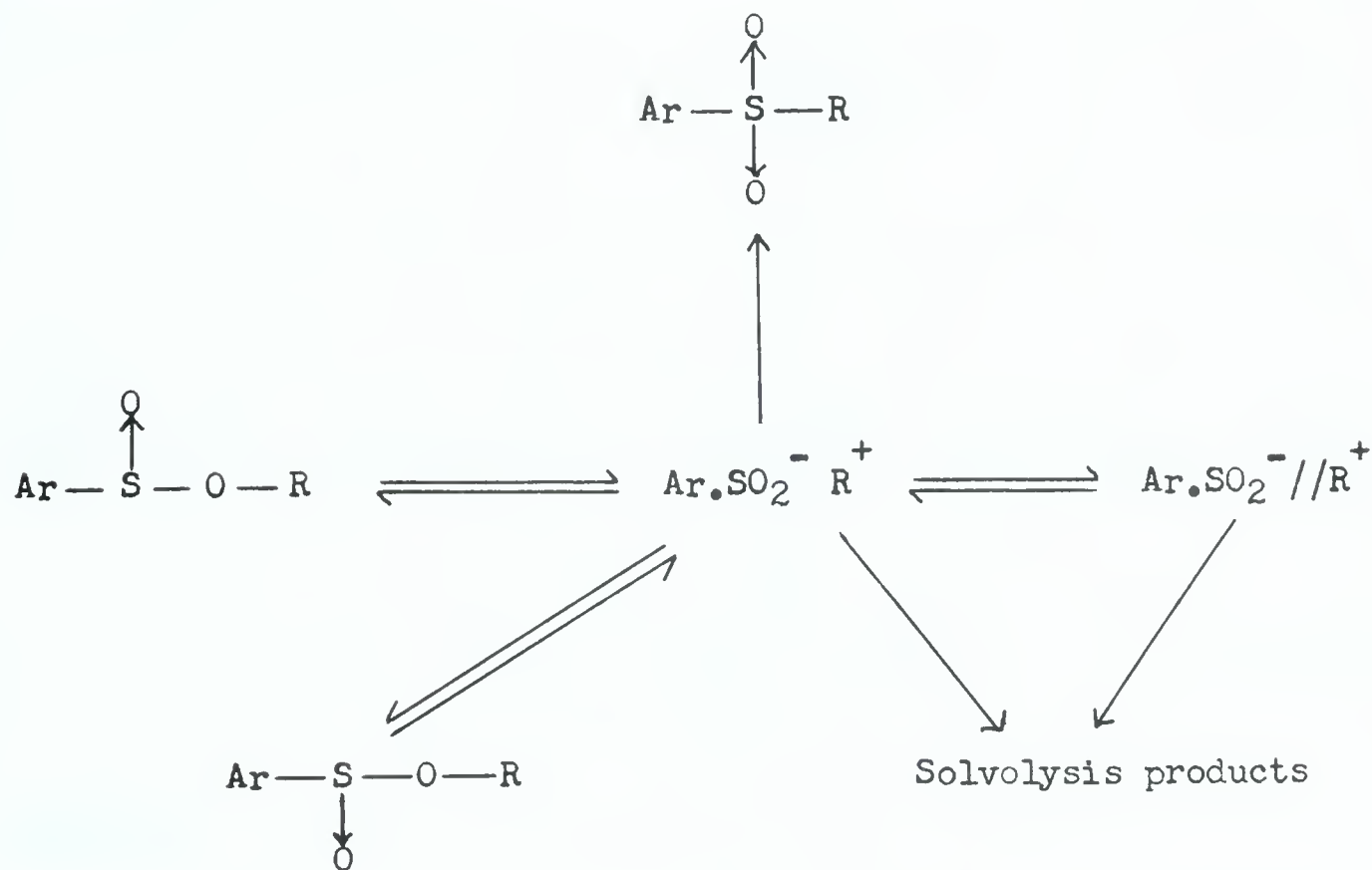
both esters. In the case of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzene-sulfinate about 30 per cent rearrangement occurs. The above argument implies that in this case about 30 per cent ion pair return to ester occurs and that the ionisation rate is at least 40 per cent greater than the measured rate of reaction. If the oxygen atoms in the sulfinate ion of an ion pair are not equivalent, the amount of ion pair return to give the starting diastereomer might be quite extensive. In this case the ionisation rate would be substantially greater than the measured rate of reaction.

In the equilibration experiments the equilibrium mixture contained 46 per cent of the fast diastereomer of each ester, corresponding to a

FIGURE XVII

The solvolysis and rearrangements of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate.

SCHEME A

$$
\begin{array}{c}
\overset{O}{\underset{O}{\overset{\uparrow}{Ar_*S}}}-R \\
\end{array}
$$

$$
\overset{O}{\underset{}{\overset{\uparrow}{Ar_*S}}}-O-R \;\rightleftharpoons\; Ar.SO_2^-\,R^+ \;\rightleftharpoons\; Ar.SO_2^-//\,R^+
$$

$$
Ar.S-O-R \qquad\qquad \text{Solvolysis products}
$$

SCHEME B

$$
\begin{array}{c}
\overset{O}{\underset{O}{\overset{\uparrow}{Ar_*S}}}-R \\
\end{array}
$$

$$
\overset{O}{\underset{}{\overset{\uparrow}{Ar_*S}}}-O-R \;\rightleftharpoons\; Ar.SO_2^-/\,R^+ \;\rightleftharpoons\; Ar.SO_2^- + R^+
$$

$$
Ar.S-O-R \qquad\qquad \text{Solvolysis products}
$$
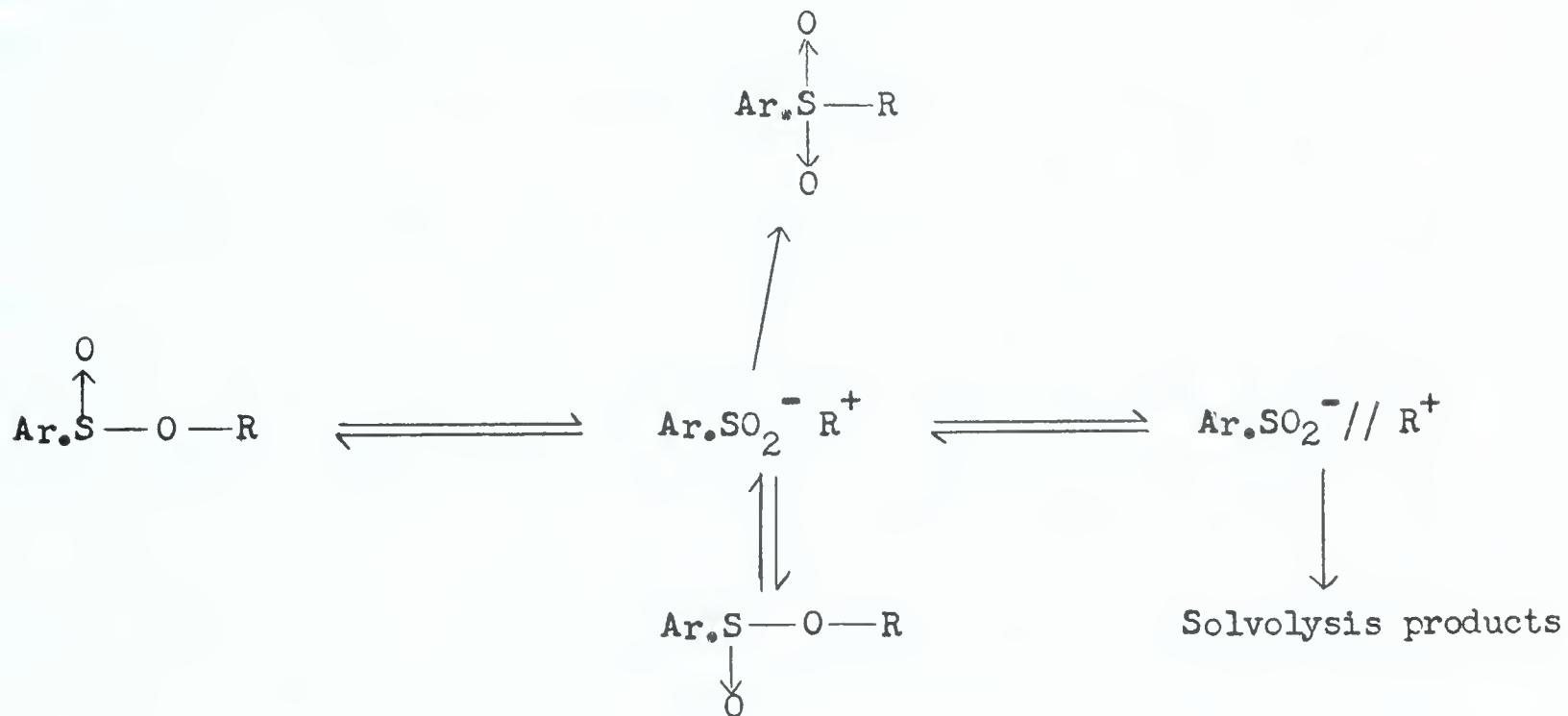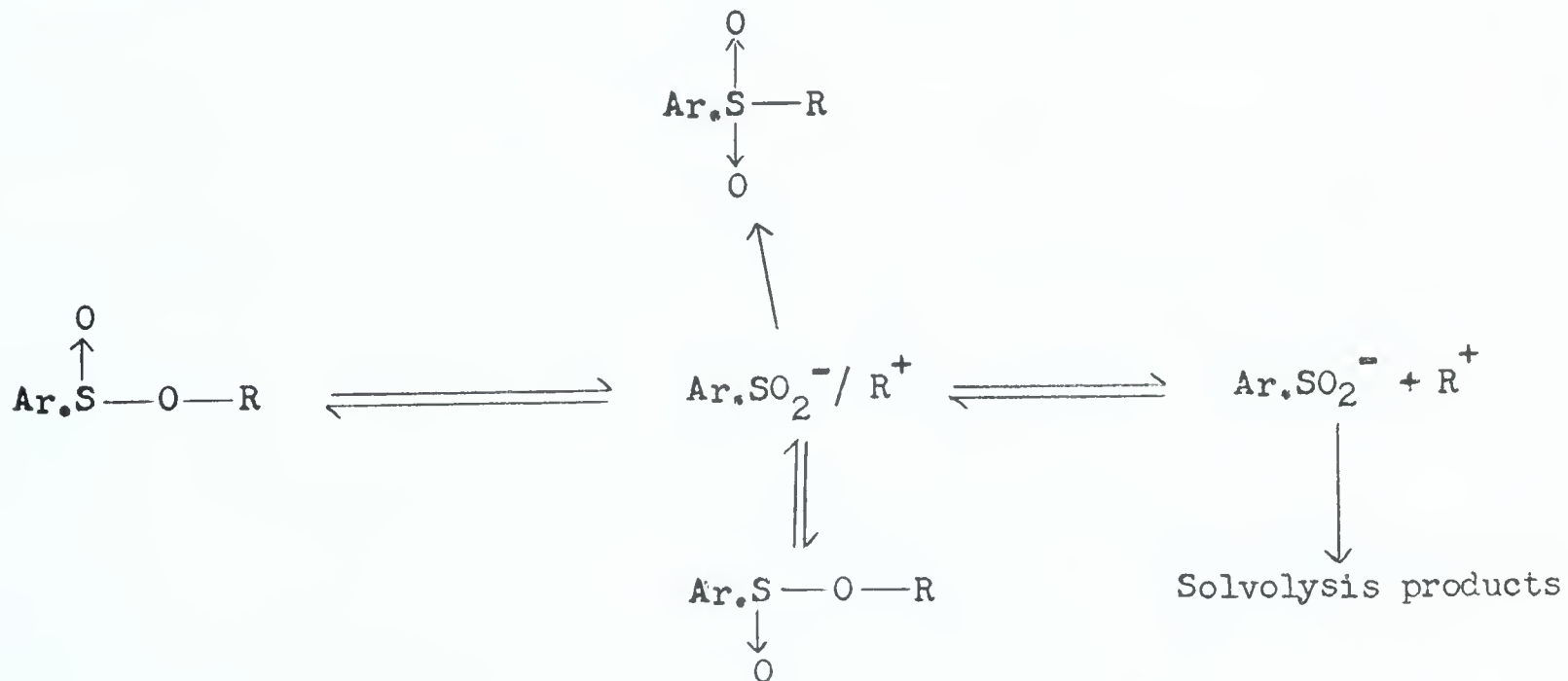
free energy difference of 95 cal. at 25°. If the energy of the transition state for the two diastereomers were equal it would be expected that the fast diastereomer would react less than 1.2 times faster than the slow diastereomer. In fact, for both esters, the rate ratio of the diastereomers is approximately 1.6, corresponding to a difference in the free energy of activation of about 330 cal. at $70-90^{\circ}$. However, the difference in ground state energy in pyridine is not necessarily the same as in hydroxylic solvents as solvation effects might be quite different. Thus one possible explanation of the apparent discrepancy between ΔF° and $\Delta\Delta F^{\ddagger}$ is simply that the measurements were carried out in different solvents. Another possible explanation is that the difference is real and the transition states for the two diastereomers differ in energy. However since the energy differences must be steric in origin it would be expected that the differences in the transition state would be less than in the ground state as bond stretching must occur. This would forecast a rate ratio of 1-1.2.

The three reactions examined in this work are the solvolysis, rearrangement to sulfone and isomerisation to a diastereomeric ester of α-arylethyl 2,6-dimethylbenzenesulfinates. The latter two reactions formally involve a three and four membered cyclic rearrangement respectively. All three reactions show the same high sensitivity to the presence of a methoxy group which is consistent with a common ionic mechanism and inconsistent with one ionic reaction and two totally different cyclic rearrangements. Ion pair return has been successfully detected by the sulfinate-sulfone rearrangement and in one case by the interconversion of diastereomeric sulfinate esters. The latter

case is equivalent to the racemisation of an optically active sulfinate

ester, Ar.SO.OR, where only the sulfur atom is asymmetric. Detection of

ion pair return by racemisation of the leaving group has not to date

been realised but the present results indicate that it should be

possible in the case of optically active sulfinate esters.

EXPERIMENTAL

Physical measurements

Melting points were taken on a Hershberg type melting point apparatus using a set of Anschutz thermometers. They were corrected by calibration of the thermometers against N. B. S. standards.

Refractive indices were measured on a Bausch and Lomb Abbe-3L refractometer which was thermostated at 25°.

Optical rotations were determined using a Rudolph Model 80 polarimeter with semi-micro polarimeter tubes. Unless otherwise stated 95 per cent ethanol was used as solvent in these measurements.

Infrared spectra were obtained on Perkin Elmer Recording Infrared Spectrophotometers, Models 21 and 421, the former being used with a four-fold expanded scale for quantitative measurements.

Nuclear Magnetic Resonance spectra were obtained on a Varian Analytical Spectrophotometer, Model A-60. Unless otherwise stated IR and NMR spectra were determined in CS_2 solution.

A Perkin Elmer Vapor Fractometer, Model 154, was utilised for vapor phase chromatographic work.

Reagents and stock solutions

Anhydrous ethanol

Anhydrous ethanol was prepared from commercial 95 per cent ethanol by initial drying with calcium oxide followed by treatment with magnesium ethoxide according to the procedure of Fieser (46). Karl Fischer

titration of the product indicated the presence of 0.003-0.004 per cent water.

Pentane

Commerical n-pentane was purified by refluxing with and distillation from phosphorus pentoxide for chromatographic use in the product analyses.

2,6-Lutidine

Practical grade (95 per cent) 2,6-lutidine was refluxed with barium oxide, distilled and stored over potassium hydroxide pellets, n_D^{25} 1.4959 (reported (66) 1.4953).

Lithium perchlorate

The trihydrate (kindly furnished by R. Mermelstein) was quantitatively dehydrated to the anhydrous salt by heating under vacuum in an Abderhalden apparatus.

Sodium azide

Sodium azide (Fischer purified) was twice recrystallised from water and dried to constant weight.

Potassium thiocyanate

Reagent grade potassium thiocyanate was recrystallised from 95 per cent ethanol and dried to constant weight.

Activated alumina

Harshaw alumina (Cat. No. AL-0109P) was activated by treatment with ethyl acetate for three days followed by washing with water and

methanol and drying under reduced pressure according to the procedure of Cope (47).

Sodium methoxide in methanol

Approximately 3g. of clean sodium was added to a gallon of anhydrous methanol and allowed to react. The solution was standardised against potassium hydrogen phthalate in water using phenolphthalein as indicator. Restandardisation showed the solution to be stable for at least three years.

Potassium thiocyanate solution

An aqueous solution of potassium thiocyanate was prepared and standardised against silver nitrate using saturated aqueous ferric ammonium sulfate in the presence of 6N nitric acid as indicator.

Potassium acetate in ethanol

An accurately weighed amount of potassium acetate was dissolved in about 600 ml. of anhydrous ethanol and about half of the ethanol distilled off to azeotrope off any water present. The solution was quantitatively transferred to a volumetric flask and made up to 500 ml. Aliquots of this solution (5 or 10 ml.) were used in the preparation of sulutions for kinetic study.

2,6-Lutidine in ethanol and 60 per cent ethanol

Accurately weighed portions of purified 2,6-lutidine were dissolved in the appropriate solvent in a volumetric flask. The solutions were used to prepare solutions for kinetic runs as described for potassium acetate.

Aqueous ethanol

Stock solutions of 60 per cent and 80 per cent ethanol were prepared by mixing three volumes of anhydrous ethanol with two volumes of boiled distilled water and four volumes of ethanol with one volume of water respectively.

Di-(o-nitrophenyl) disulfide (19,20)

A solution of 360 g. (4.6 moles) of dry sodium sulfide and 48 g. (1.5 moles) of sulfur in 1.5 litres of 95 per cent ethanol in a 3 l. round bottom flask was prepared by warming and added slowly to a solution of 315 g. (2.0 mole) of o-nitrochlorobenzene in 500 ml. of ethanol in a 5 l. round bottom flask. After heating for six hours on the steam bath the mixture was cooled, the disulfide collected by filtration, stirred with 500 ml. of water to remove sodium chloride and washed with ethanol, yield 160 g. (52 per cent), m.p. 187-191° (reported (19) m.p. 192-195°).

o-Nitrobenzenesulfonyl chloride (21,22)

Di-(o-nitrophenyl) disulfide (50 g., 0.16 moles) was stirred with 250 ml. of concentrated HCl and 50 ml. of concentrated HNO_3, warmed to 70° and chlorine passed in very slowly. After 90 min., the acid chloride was separated by decanting the supernatent liquid without cooling and allowed to crystallise. The product was used in the subsequent step without further purification, yield 57 g. (79 per cent), m.p. 66-69° (reported m.p. 64-65° (21), 67-69° (22)), infrared (Nujol) 1530, 1380, 1355, 1180 cm.$^{-1}$.

Hydrazine reduction (23)

A solution of 14.6 g. (0.066 moles) of o-nitrobenzenesulfonyl chloride in 30 ml. of benzene was added over a period of ten minutes to a solution of 10 g. (0.2 moles) of hydrazine hydrate in 40 ml. of ethanol with thorough manual shaking. The solution was allowed to warm up to 60° and after brisk nitrogen evolution had ceased was kept at 60° for one hour. The solution was allowed to stand at room temperature for five hours, the mass of needles which separated was removed by filtration and the filtrate evaporated to dryness. Dilute HCl was added to the residue, which was then ether extracted. The ether solution was washed with water and the solvent removed under reduced pressure to yield 8 g. of o-nitrobenzenesulfinic acid. The acid was dissolved in aqueous sodium carbonate with heating and removal of some insoluble material by filtration. On cooling, the solution gave a doposit of orange needles which were collected by filtration and dissolved in a small amount of water. Addition of dilute HCl precipitated the acid, yield 6 g. (50 per cent), m.p. 110-115° (reported m.p. 134° (23), 138-139° (24)), infrared (Nujol) 1430, 1355, 1075 cm.$^{-1}$.

Stannous chloride reduction (24)

A solution of onitrobenzenesulfonyl chloride (80 g., 0.36 moles) in one litre of ethanol in a three litre erlenmeyer was prepared. A solution of 35 ml. (0.43 moles) of concentrated HCl and 90 g. (0.48 moles) of stannous chloride in 400 ml. ethanol was added gradually, keeping the temperature below 30°. Water (100 ml.) was then added, followed by 150 g. of sodium carbonate. The mixture was stirred until the solution was no longer acid and excess sodium carbonate removed by

filtration. The volume of the solution was reduced to about 400 ml. and cooled to yield 40 g. of sodium o-nitrobenzenesulfinate which was dissolved in water. The addition of dilute HCl gave o-nitrobenzene-sulfinic acid, yield 27 g. (40 per cent), m.p. 110-115°. In other preparations using the same procedure yields of up to 60 per cent were obtained. The infrared spectrum of the product was identical with that of the product from the hydrazine reduction.

o-Nitrobenzenesulfonyl chloride from o-nitrobenzenesulfinic acid (25)

o-Nitrobenzenesulfinic acid (2 g., 0.01 moles) was warmed to 70° with 75 ml. of water and chlorine bubbled in. The oil which formed initially solidified on cooling, yield 1.5 g (70 per cent), m.p. 65-69°. The infrared spectrum was identical with that of the o-nitro-benzenesulfonyl chloride described above.

α-Phenylethyl o-nitrobenzenesulfinate

Thionyl chloride (35 ml., 94 g., 0.79 moles) and o-nitrobenzene-sulfinic acid (25 g., 0.13 moles) were refluxed together for one hour and the excess thionyl chloride removed at reduced pressure overnight. The residue was dissolved in 75 ml. of anhydrous pyridine, cooled to 0° and 16 g. (0.13 moles) of α-phenylethanol added. After 50 hours at 0° the mixture was poured on to excess ice-HCl and extracted with 400 ml. of ether. The ether solution was washed with water until the washings were colorless, the volume reduced and pentane added. Cooling in dry ice-acetone yielded 8.8 g. of crude α-phenylethyl o-nitrobenzene-sulfinate which was recrystallised from ether-Skelly Solve B, yield 2.8 g. (7.4 per cent), m.p. 67-68.5°, infrared (Nujol) 1525, 1340, 1120,

865 cm.$^{-1}$. The compound decomposed after two to three weeks at room temperature.

Solvolysis of α-phenylethyl o-nitrobenzenesulfinate in ethanol

α-Phenylethyl o-nitrobenzenesulfinate (0.927 g., 0.00318 moles) and sodium acetate (0.470 g., 0.00583 moles) were dissolved in dry ethanol in a volumetric flask and the volume made up to 100 ml. The solution was transferred to a 250 ml. round botton flask and refluxed. At intervals it was allowed to cool to room temperature and 5 ml. aliquots withdrawn using an automatic pipette. These were delivered into an ether-water mixture, shaken, the ether layer washed three times with water, dried with magnesium sulfate and the ether removed at reduced pressure. The residue was dissolved in CS_2 and the infrared spectrum taken.

A solution of α-phenylethyl o-nitrobenzenesulfinate (1.015 g., 0.0035 moles) and sodium acetate (0.485 g., 0.0059 moles) in 100 ml. of ethanol was refluxed for 48 hours. It was then poured into water, extracted with ether, the ethereal solution washed with water and dried. After removal of the ether, the residue was dissolved in ethanol and Skelly Solve B added, yield of ethyl o-nitrobenzenesulfinate 0.280 g. (37 per cent), m.p. 52.5-54.5°, infrared 1335, 1140, 880 cm.$^{-1}$.

α-Phenylethanol

Lithium aluminum hydride (16 g., 0.42 moles) was cautiously crushed and placed in a one litre three-necked flask fitted with a stirrer, condenser and dropping funnel. Ether (200 ml.) was then added and a solution of 100 g. (0.83 moles) of acetophenone in 200 ml. of

ether added dropwise at such a rate as to cause gentle reflux. When

the addition was complete 32 ml. of water was added carefully followed

by 29 ml. of 10 per cent sodium hydroxide. The ether layer was separated

by decantation and the residue washed several times with ether. The

combined ether extracts were washed once with water, dried with magnesium

sulfate and the solvent removed at reduced pressure. The yield of

α-phenylethanol was practically quantitative, n_D^{25} 1.5248, m.p. 6-13°

(reported n_D^{25} 1.5244 (67), m.p. 19-20° (68)), infrared 3605, 1070, 760

695 cm.$^{-1}$, n.m.r. 2.85(s), 550 (q), 6.12(s), 8.79τ(d), ratio 5:1:1:3

(calculated 5:1:1:3). Where n.m.r. data are reported s = singlet,

d = doublet, t = triplet, q = quartet, m = multiplet.

α-(p-methoxyphenyl)ethanol

This compound was prepared by lithium aluminum hydride reduction

of p-methoxyacetophenone by the method described above for α-phenyl-

ethanol, n_D^{25} 1.5291 (reported (49) n_D^{25} 1.5310), infrared 3595, 1260,

1050, 835 cm.$^{-1}$, n.m.r. 3.2(m), 5.47(q), 6.39(s), 8.77τ(d), ratio

4:1:4:3 (calculated 4:1:(1+3):3).

2,6-Dimethylbenzenesulfinic acid (26)

2,6-Dimethylaniline (25 g., 0.21 moles) was dissolved in a cold

mixture of 550 ml. of water and 150 ml. of sulfuric acid in a 2 litre

erlenmeyer. The solution was cooled in an ice-salt bath and a solution

of 17 g. (0.25 moles) of sodium nitrite in 100 ml. of water added

gradually with mechanical stirring, keeping the temperature below 5°.

When the addition was complete SO_2 was bubbled in for at least an hour

and the mixture transferred to a 3 or 4 litre beaker. Copper powder

-114-

(200 g.) was added gradually while the cooling and SO_2 addition were continued. The cooling bath containing the beaker was allowed to warm up to room temperature while SO_2 addition was continued. The mixture was then filtered and the residue washed with a little cold water. The residue, which consisted of a mixture of copper and sulfinic acid, was added gradually to excess 10 per cent sodium carbonate in a 3 litre beaker and filtered. The filtrate was cooled in ice and acidified with cold 50 per cent sulfuric acid. The precipitated 2,6-dimethylbenzene-sulfinic acid was collected, washed with a little water and air dried overnight, yield 25-30 g. (74-88 per cent), m.p. 91° (reported (36) m.p. 92-94°), infrared (Nujol) 2080 (broad), 1050, 995, 820 cm.$^{-1}$. It was recrystallised from wet ethanol, m.p. 94-95.5^o.

2,6-Dimethylbenzenesulfinyl chloride

A typical preparation is described. Thionyl chloride (10 ml., 27 g., 0.23 moles) was dissolved in 50 ml. of pentane and 10 g. (0.059 moles) of 2,6-dimethylbenzenesulfinic acid added gradually, in a 125 ml. erlenmeyer. When the reaction was complete a small tarry residue was removed by filtration and the pentane and excess thionyl chloride removed overnight at reduced pressure. The acid chloride was used for the preparation of esters without purification.

2,6-Dimethylbenzenesulfinates

The same procedure was used for the preparation of all 2,6-dimethyl-benzenesulfinates. A typical procedure for the preparation of α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate is given as an example.

The acid chloride obtained from 7 g. (0.041 moles) of 2,6-dimethyl-benzenesulfinic acid was dissolved in 15 ml. of anhydrous pyridine in a 125 ml. filter-flask, and the solution cooled in dry ice-acetone until crystallisation commenced. A solution of 5.5 g. (0.036 moles) of ∝-(p-methoxyphenyl)ethanol in 15 ml. of anhydrous pyridine was added. The mixture was allowed to warm to 0° and poured on to a mixture of ice and 35 ml. of conc. HCl. The mixture was twice extracted with ether and the combined ether extracts washed first with water, then with 10 per cent sodium carbonate until the washings were colorless and finally with water again. The solution was dried over magnesium sulfate and the solvent removed at room temperature.

The procedure for each individual ester will be described from this stage.

Ethyl 2,6-dimethylbenzenesulfinate

The ester crystallised after removal of the solvent and was recrystallised from ether, m.p. 46-48° (reported (2) m.p. 47.3-48.6°). The infrared spectrum was superimposable on that of an authentic specimen supplied by R. Mermelstein.

∝-Phenylethyl 2,6-dimethylbenzenesulfinate

Partial crystallisation occurred on removal of the solvent. Enough cold pentane-ether mixture was added to dissolve the non-crystalline material and the crystals were collected quickly by filtration. Recrystallisation from ether-pentane gave diastereomerically pure ∝-phenylethyl 2,6-dimethylbenzenesulfinate, m.p. 65.5-67.5°, infrared 1135, 880, 770, 700 cm.$^{-1}$, n.m.r. 2.80(s) + 3.1(m), 4.79(q), 7.59(s),

8.46$\mathcal{T}$(d), ratio 8:1:6:3 (calculated 8:1:6:3), n.m.r. (pyridine)

4.47(q), 7.45(s), 8.40$\mathcal{T}$(d), ratio 1:6:3 (calculated 1:6:3).

Calculated for $C_{16}H_{18}O_2S$, S 11.69 per cent, found S 11.45, 11.83

per cent.

By reduction of the volume and cooling crystallisation from the

mother liquors could be effected. The product had m.p. 39-41°, n.m.r.

281(s) + 2.1(m), 4.76(q), 7.51 + 7.60(2 singlets), 8.46$\mathcal{T}$(d), ratio

8:1:6:3 (calculated 8:1:6:3), n.m.r. (pyridine) 4.48(q), 7.35 + 7.45

(2 singlets), 8.41$\mathcal{T}$(2 doublets), ratio 1:6:3 (calculated 1:6:3).

α-(p-Methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate

Partial crystallisation occurred on removal of the solvent. The

ester was washed with a little ether and recrystallised from ether or

ether-pentane, m.p. 69-71°, infrared 1245, 1130, 1030, 865, 770 cm.$^{-1}$,

n.m.r. 3.1(m), 4.86(q), 6.39(s) 7.63(s) 8.49$\mathcal{T}$(d), ratio 7:1:3:6:3

(calculated 7:1:3:6:3), n.m.r. (pyridine) 4.55(q) 6.38(s), 7.47(s),

8.48$\mathcal{T}$(d), ratio 1:3:6:3 (calculated 1:3:6:3). Calculated for $C_{17}H_{20}O_3S$,

S 10.53 per cent, found S 10. 63 per cent.

The ether was removed from the original washing, n.m.r. 3.1(m),

4.88(q), 6.38(s), 7.54 + 7.63(2 singlets), 8.47$\mathcal{T}$(d), ratio 7:1:3:6:3

(calculated 7:1:3:6:3). Minor peaks were also present at 7.74, 7.93,

8.69 and 8.79$\mathcal{T}$. The first two peaks are present in the spectrum of

2,6-dimethylphenyl 2,6-dimethylbenzenethiolsulfonate. The infrared

spectrum was superimposable on that of the pure ester, except for a weak

peak at 1330 cm.$^{-1}$ due to thiolsulfonate.

α-Phenylethyl chloride (27)

α-Phenylethanol (8 g., 0.066 moles) was added gradually to 20 g. (0.17 moles) of thionyl chloride at room temperature. The mixture was allowed to stand for 30 minutes and fractionally distilled, yield 7 g. (80 per cent, b.p. 79-81° at 18 mm., n_D^{25} 1.5233 (reported (27) b.p. 85° at 20 mm., (69) n_D^{17} 1.5277), n.m.r. 2.80(s), 5.11(q), 8.27τ(d), ratio 5:1:3 (calculated 5:1:3).

2,6-Dimethylthiophenol (28)

2,6-Dimethylaniline (90 g., 0.74 moles) was slowly added with mechanical stirring to a mixture of 150 ml. of hydrochloric acid and 150 g. of ice in a one litre erlenmeyer. A solution of 55 g. (0.80 moles) of sodium nitrite in 125 ml. of water was added, keeping the temperature below 5°. A solution of 140 g. (0.87 moles) of potassium ethyl xanthate in 180 ml of water in a 2 litre round bottom flask was warmed to 40° and the cold diazonium salt solution added gradually with stirring, maintaining the temperature about 40°. The mixture was left until the xanthate separated as a red oil. The aqueous layer was removed by decantation and twice extracted with 100 ml. portions of ether. The combined oil and ether extracts were washed with 100 ml. of 10 per cent sodium hydroxide and 100 ml. of water, dried with magnesium sulfate and the ether removed at the aspirator. The crude xanthate was dissolved in 500 ml. of ethanol in a 1 litre round bottom flask, heated to boiling point, 175 g. (3.1 moles) of potassium hydroxide pellets added at such a rate as to maintain boiling and refluxed over-night. Most of the ethanol was distilled off, the residue taken up in the minimum amount of water and washed three times with 100 ml. portions

of ether. The solution was made strongly acid with 6N sulfuric acid,

placed in a three litre round bottom flask, 2 g. of zinc dust added and

steam distilled, yield 10-30 per cent, b.p. 90-93$^{\mathrm{o}}$ at 13 mm. n_D^{25} 1.5703

(reported (36) b.p. 74-75$^{\mathrm{o}}$ at 6 mm., n_D^{25} 1.5687). The infrared

spectrum was superimposable on that of an authentic sample (kindly

supplied by S. Braverman).

α-Phenylethyl 2,6-dimethylphenyl sulfide (37)

A solution of α-phenylethyl chloride (1.5 g., 0.01 moles),

2,6-dimethylthiophenol (1.5 g., 0.012 moles) and sodium hydroxide (0.5

g., 0.012 moles) in 50 ml. of 98 per cent ethanol was refluxed for

five hours. The solution was poured into water, ether extracted, the

ether extract washed with water and dried with magnesium sulfate.

Removal of the ether at the aspirator yielded 2.2 g. (90 per cent)

of α-phenylethyl 2,6-dimethylphenyl sulfide, infrared 1370, 1190,

1020, 760, 690 cm.$^{-1}$.

α-Phenylethyl 2,6-dimethylphenyl sulfoxide

A cold solution of 0.9 g. (0.009 moles) of chromium trioxide in

25 ml. of acetic acid was prepared, 1.5 g. (0.006 moles) of α-phenyl-

ethyl 2,6-dimethylphenyl sulfide added and the solution left overnight

at room temperature in a stoppered 50 ml. erlenmeyer. The solution was

poured into water, ether extracted, the ether extract washed with water

and 10 per cent sodium carbonate, dried over sodium carbonate and the

solvent removed at the aspirator, yield 0.340 g., m.p. 105-108$^{\mathrm{o}}$. The

product was recrystallised from Skelly Solve B, m.p. 110-112$^{\mathrm{o}}$, infra-

red 1110, 1055, 750, 690 cm.$^{-1}$.

⍺-Phenylethyl 2,6-dimethylphenyl sulfone

⍺-Phenylethyl 2,6-dimethylphenyl sulfide (2.9 g., 0.020 moles)
was dissolved in 50 ml. of acetic acid and 5 ml. (0.44 moles) of 30 per
cent hydrogen peroxide added and the solution left overnight in the dark.
The solution was poured into water, ether extracted, the ether extract
washed with water and 10 per cent sodium carbonate, dried over sodium
carbonate and the solvent removed at the aspirator. The crude sulfone
was recrystallised from ethanol, yield 1.5 g. (50 per cent), m.p. 134.5-
135.5°, infrared 1310, 1145, 1120, 770, 690, 630 cm.$^{-1}$, n.m.r. 3.0(m),
5.89(q), 7.66(s), 8.30τ (d), ratio 8:1:5.5:3 (calculated 8:1:6:3).

Expected for $C_{16}H_{18}O_2S$ C 70.04%   H 6.61%   S 11.69%

Found   C 70.00%   H 6.51%   S 11.76%
                                  69.82%   6.55%

⍺-(p-Methoxyphenyl)ethyl 2,6-dimethylphenyl sulfone (29)

⍺-(p-Methoxyphenyl)ethanol (5 g., 0.033 moles) was dissolved
in 100 ml. of 98 per cent formic acid which had been treated with 5 g.
(0.047 moles) of sodium carbonate. The solution was stirred with a
magnetic stirrer in a 250 ml. erlenmeyer with 7 g. (0.041 moles) of
2,6-dimethylbenzenesulfinic acid. After $2\frac{1}{2}$ hours the precipitate which
formed was collected by filtration. It was dissolved in methylene
chloride, washed with water, dried over p otassium carbonate and the
solvent removed at the aspirator, yield 2 g., m.p. 113-114°. After a
total reaction time of three hours the formic acid solution was poured
into water, the precipitate collected, washed with water and 10 per
cent sodium carbonate and air dired overnight, yield 5.7 g., m.p.
109.5-112°. The two fractions were combined and recrystallised from

ether, yield 5.5 g. (54 per cent), m.p. 116-117°, infrared 1315, 1250,
1150, 830, 775 cm.$^{-1}$, n.m.r. 3.2(m), 5.98(q), 6.34(s), 7.68(s),
8.37$\mathcal{T}$(d), ratio 7:1:3:6:3 (calculated 7:1:3:6:3).

Expected for $C_{17}H_{20}O_3S$ C 67.07%   H 6.62%   S 10.53%

Found   C 66.97%   H 6.62%   S 10.54%
                                      67.12%   6.64%

Lambert-Beer Law and extraction procedure controls

A typical procedure will be described. The procedure in other
cases differed only in the compound and solvents used.

α-(p-Methoxyphenyl)ethyl 2,6-dimethylphenyl sulfone (0.2898 g.,
0.0009462 moles) was weighed out in a 100 ml. volumetric flask,
dissolved in ethanol and the solution made up to the mark. Using a
calibrated automatic pipette 20, 15, 10 and 5 ml. portions of the
solution were transferred to four 25 ml. volumetric flasks. These
were filled to the mark with ethanol to give solutions of the concen-
trations listed in Table IV. Aliquots (5 ml.) of these solutions were
extracted as described for the kinetic runs, the solvent removed at
reduced pressure and 1 ml. of CCl_4 added using an automatic pipette.
The optical density at 7.65μ was measured and plotted against concen-
tration.

Data for the Lambert-Beer plots in other cases are given in
Tables XLI to XLIV.

Kinetic procedure

The ester, base and salt, if applicable, were dissolved in the
appropriate solvent in a 50 or 100 ml. volumetric flask. In some cases
a 5 ml. aliquot was withdrawn with a calibrated automatic pipette and

TABLE XLI

Relationship between concentration and optical density at 7.65μ in

CCl$_4$ for α-phenylethyl 2,6-dimethylphenyl sulfone

[Sulfone]	log I_0/I	[Sulfone]	log I_0/I
0.005117M	0.5919	0.002047M	0.2495
0.003070	.3635	0.001023	.1340
0.002559	.3108		

TABLE XLII

Relationship between concentration and optical density at 11.45μ in

bromoform for α-phenylethyl 2,6-dimethylbenzenesulfinate

[Ester]	log I_0/I	[Ester]	log I_0/I
0.02393M	0.8726	0.00831M	0.2872
0.01661	0.6059	0.00416	0.1373

TABLE XLIII

Relationship between concentration and optical density at 4.80μ in

CCl$_4$ for α-phenylethyl azide

[Azide]	log I_0/I	[Azide]	log I_0/I
0.02293M	1.3410	0.009172M	0.5151
.01834	1.0088	.004586	.2491
.01376	0.8224	.002293	.0763
.01147	0.5957		

TABLE XLIV

Relationship between concentration and optical density at 4.80 μ in

CCl$_4$ for α-(p-methoxyphenyl)ethyl azide

[Azide]	log I$_0$/I	[Azide]	log I$_0$/I
0.02237M	1.3802	0.006710M	0.5885
.01790	1.2952	.004474	0.3915
.01342	1.0574	.01548	1.1163
.01119	0.8840	.009288	0.7588
.008948	0.7498	.003096	0.2673

analysed in the same way as the other points. The remaining solution

was pipetted into ampoules (5.5-6 ml. in each) and the ampoules sealed.

They were placed in a basket in the appropriate constant temperature

bath and withdrawn at intervals, the zero point being taken after three

minutes had been allowed for equilibration. The reaction was quenched

by placing the tube in a beaker containing ice-water. The tube was

then equilibrated to 25° and a 5 ml. aliquot withdrawn using a cali-

brated automatic pipette.

Rates were measured on the p-methoxy ester by pipetting the

solution into 25 ml. of pentane and 10 ml. of boiled distilled water

in a 60 ml. separatory funnel. The funnel was shaken approximately 50

times and the aqueous layer separated. The solution was then extracted

with a further 10 ml. portion of boiled distilled water and the combined

extracts titrated with sodium methoxide using ca. 20 drops of phenol-

phthalein as indicator. For infinity measurements the pentane solution

was then washed with 10 ml. portions of 3N HCl and water (twice), dried

- 123 -

with granular anhydrous sodium or potassium carbonate, transferred to a 50 ml. pear shaped flask and the solvent removed. The appropriate solvent for infrared measurement was then added.

Infrared rate measurements on the unsubstituted ester were carried out using the procedure described above for infinity measurements with the exception that in most cases the first two washings were not titrated. Titrimetric rate constants were obtained by pipetting 5 ml. of the solution directly into 20 ml. of boiled distilled water and titrating with sodium methoxide using phenolphthalein as indicator.

For rate measurements at 25° the reaction was conducted in a stoppered volumetric flask and the reaction quenched by pipetting into pentane. In all cases where the added base was sodium or potassium acetate the washing with dilute HCl during the extraction procedure was replaced by washing with water. Polarimetric rates were measured directly on the reaction mixture after quenching with ice-water and equilibration to room temperature. Infinities were taken after at least ten half-lives.

Stability of 2,6-dimethylbenzenesulfinic acid in 60% ethanol at 90°

2,6-Dimethylbenzenesulfinic acid (0.5074 g., 0.002981 moles) was weighed out in a 100 ml volumetric flask, 10 ml. of 0.9649M 2,6-lutidine in ethanol added using an automatic pipette and the solution made up to the mark with ethanol. Titrations were carried out as for kinetic runs with α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate in this solvent. The results are listed in Table IX.

α-Phenylethyl ethyl ether

Method A (3)

Powdered potassium was prepared in xylene (51) and transferred to ether by repeated decantations. The powdered potassium (2 g., 0.051 moles) was allowed to react with 6.1 g. (0.049 moles) of α-phenylethanol in 50 ml. of ether in a 100 ml. round bottom flask fitted with a condenser. A solution of 6 g. (0.055 moles) of ethyl bromide in 15 ml. of ether was added and the mixture sitrred overnight using a magnetic stirrer. The mixture was filtered and the solution fractionally distilled, yield 3.5 g. (45 per cent), b.p. 62° at 13 mm., n_D^{25} 1.4857 (reported (3) b.p. 67° at 14 mm., (70) n_D^{25} 1.4846). Gas liquid chromatography showed the presence of minor impurities in the compound prepared in this manner which were difficult to remove.

Method B (42)

A mixture of 26 g. (0.21 moles) of α-phenylethanol and 30 g. (0.62 moles) of sodium hydride-mineral oil (50 per cent by weight) in 500 ml. of ether in a 1 litre three-necked flask was stirred for 2 days, 110 g. (1.01 moles) of ethyl bromide added and the stirring continued for a further 5 days. A 1:1 mixture of ether and methanol was then added cautiously until no further exothermic reaction occurred. Saturated ammonium chloride solution was added to precipitate the inorganic salts, the ethereal solution removed by decantation and the residue twice extracted with 250 ml. portions of ether. The combined ether solutions were washed with saturated sodium chloride, dried over magnesium sulfate and fractionally distilled, the fraction boiling at

-125-

73-77° at 13 mm. being collected (reported (3) b.p. 67° at 14 mm.).

The remainder of the product was α-phenylethanol and minor quantities

of this compound in the distillate were removed by chromatography on

alumina, yield 12 g. (35 per cent), n_D^{25} 1.4774 (reported (70) n_D^{25} 1.4846),

infrared 1375, 1105, 760, 700 cm.$^{-1}$, n.m.r. 2.81(s), 5.72(q), 6.75(q),

8.59(d) + 8.90$\mathcal{T}$(t), ratio 5:1:2:6 (calculated 5:1:2:6). A single peak

was observed in gas liquid chromatography.

Gas Liquid Chromatographic analysis

Perkin-Elmer Column K (Carbowax) was used at 175° and a helium

pressure of 30 p.s.i.. Peak areas were measured by the product of peak

height and retention time as the peak widths for styrene and α-phenyl-

ethyl ethyl ether were too small to allow convenient measurement by any

other method.

The standardisation procedure was as follows. Mixtures of

α-phenylethanol, α-phenylethyl ethyl ether, styrene and acetophenone

of varying composition were accurately weighed out. Approximately 5 ml.

of purified pentane was added to each mixture and 7-9 μl of the solution

injected. Plots of the peak areas relative to α-phenylethanol against

the mole ratio are shown in Figures XVIII and XIX.

In the control run three solutions of α-phenylethanol and

α-phenylethyl ethyl ether in 60 per cent ethanol were prepared. 5 Ml.

of each solution was added using an automatic pipette to 10 ml. of

methylene chloride and 5 ml. of water in a 60 ml. separatory funnel and

shaken. The methylene chloride layer was separated, dried over magnesium

sulfate, transferred to a 50 ml. pear shaped flask and the bulk of the

methylene chloride evaporated through two 18" Vigreaux columns, which

$$X = C_6H_5 \cdot \overset{\overset{\text{O}}{\|}}{C} \cdot CH_3$$
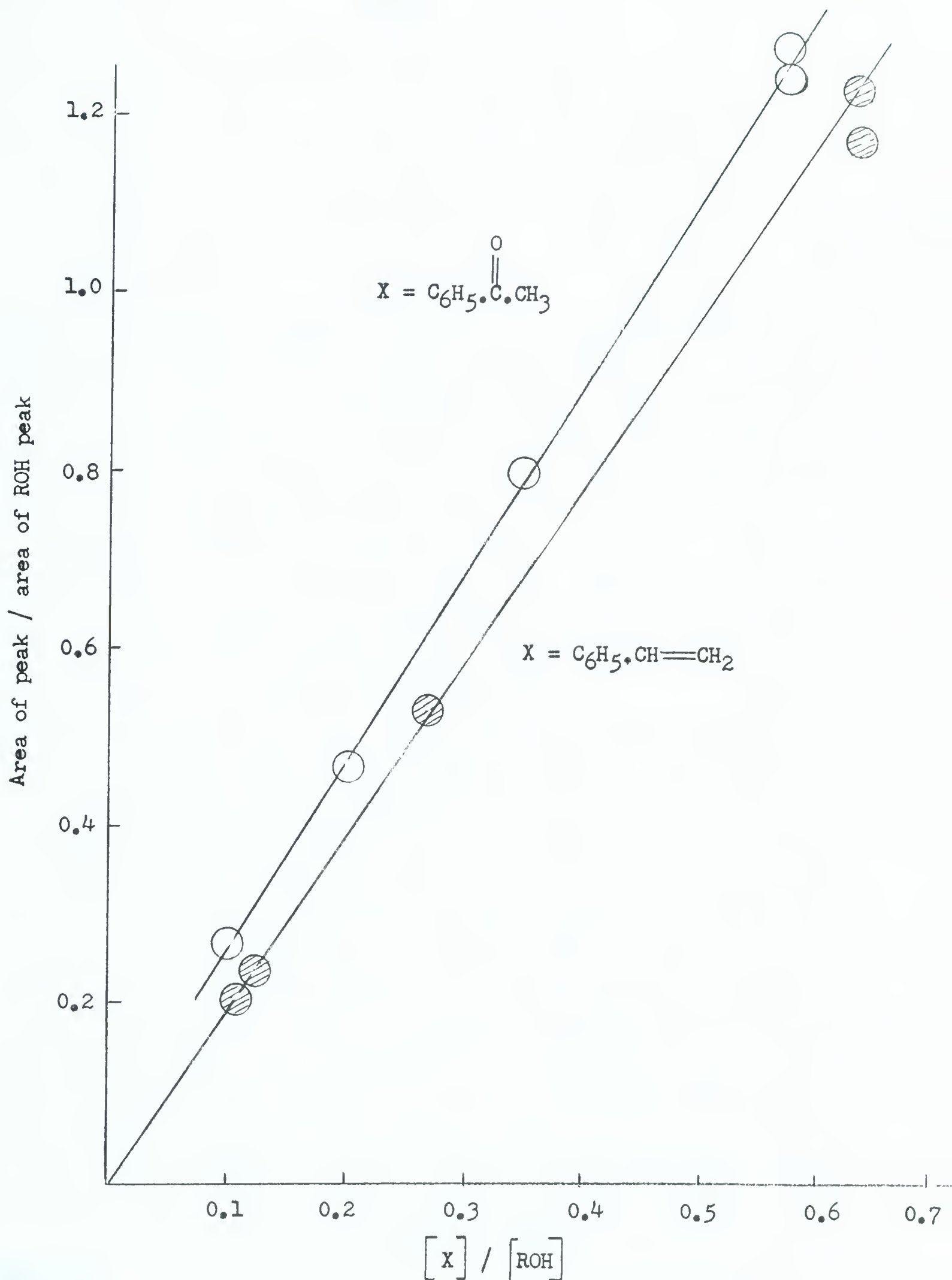
$$X = C_6H_5 \cdot CH = CH_2$$

FIGURE XVIII

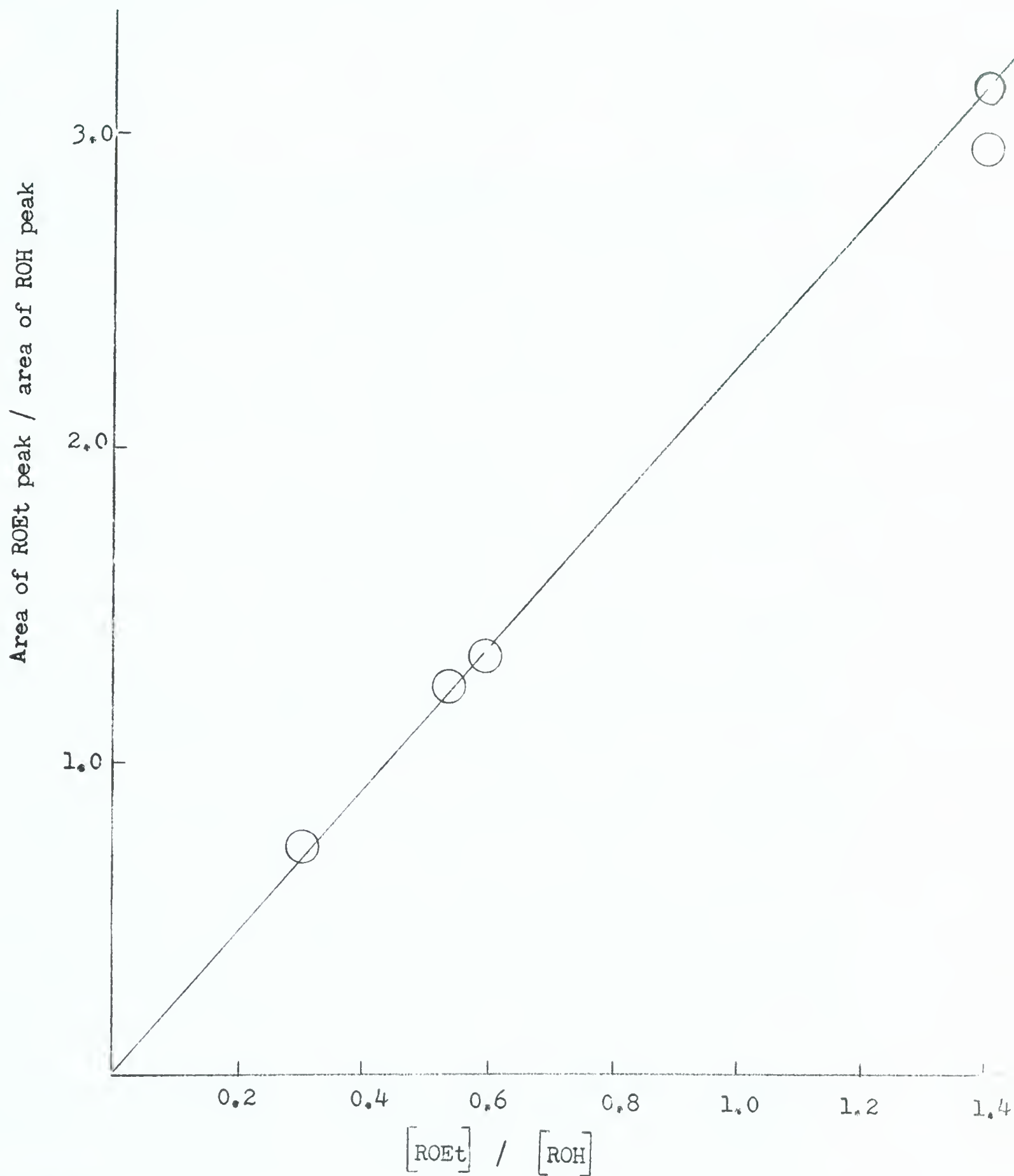Standardisation of gas liquid chromatographic analysis of styrene, acetophenone and ∝-phenylethanol.

FIGURE XIX

Standardisation of gas liquid chromatographic analysis of ⍺-phenylethyl

ethyl ether and ⍺-phenylethanol.

were allowed to drain back into the flask. Gas liquid chromatographic

analysis yielded the data of Table XV.

The same procedure was used for the analyses reported in the

results section.

Isolation of the products from the rearrangement and solvolysis of

α-phenylethyl 2,6-dimethylbenzenesulfinate in 60% ethanol.

A typical experiment is described (Run 2-161). α-Phenylethyl

2,6-dimethylbenzenesulfinate (1.0038 g., 0.003658 moles) was weighed out

in a 100 ml. volumetric flask, 10 ml. of 0.9696M 2,6-lutidine in 60 per

cent ethanol added using an automatic pipette, made up to the mark with

60 per cent ethanol and shaken until dissolved. The solution was trans-

ferred to a 170 ml. pressure bottle and allowed to react at 90° for

10 days (12 half-lives). After cooling to room temperature the solution

was poured into 200 ml. of methylene chloride in a 500 ml. separatory

funnel and the organic layer washed successively with 100 ml. water,

100 ml. 3N HCl and 100 ml. water. The solution was dried with magnesium

sulfate and the solvent removed through two 18" Vigreaux columns which

were allowed to drain back into the flask. About 200 ml. of purified

pentane was added and the mixture chromatographed on 15 g. of activated

alumina taking 200 ml. cuts. The solvent was removed from the chroma-

tographic fractions through two 18" Vigreaux columns as before. In the

case of the α-phenylethyl ethyl ether fractions the last few ml. of

solvent was removed by blowing a gentle stream of air on the surface

of the solution for the minimum time required to remove the solvent.

Solvent was removed from the other fractions at reduced pressure.

The results of the chromatography are presented in Table XLV.

TABLE XLV

Chromatography of products from the solvolysis and rearrangement of

α-phenylethyl 2,6-dimethylbenzenesulfinate in 60% ethanol

Eluant	Wt. of residue	Compound
$CH_2Cl_2-C_5H_{12}$	0.131 g.	ROEt
1%$Et_2O-C_5H_{12}$	0.036 g.	"
"	0.004 g.	"
10%$Et_2O-C_5H_{12}$	0.079 g.	$ArSO_2R$
"	0.036 g.	"
"	0.001 g.	"
Et_2O	0.197 g.	ROH
"	0.036 g.	"
"	0.001 g.	"

Isolation of the products from the reaction of α-(p-methoxyphenyl)-

ethyl 2,6-dimethylbenzenesulfinate in ethanol at 70°

α-(p-Methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate (1.7458 g.,

0.005699 moles) was weighed out in a 250 ml. volumetric flask, 50 ml.

of 0.5322M potassium acetate in ethanol added and the solution made up

to the mark with ethanol. It was transferred to two 170 ml. pressure

bottles and allowed to react for 194 min. (11 half-lives) at 70°. After

cooling, the solution was poured into 1 litre of ether, the ethereal

layer washed five times with 100 ml. portions of water, dried over

magnesium sulfate and the ether removed through a Vigreaux column.

Partial cyrstallisation occurred and the sulfone was washed by decanta-

tion with three 20 ml. portions of pentane, yield 0.484 g. (27.7 per cent),

m.p. 114.5-115.5°. A further 0.028 g. (1.6 per cent) of sulfone was

isolated by cooling the combined pentane solutions. Removal of the

pentane at reduced pressure yielded 0.737 g. (72.1 per cent) of

α-(p-methoxyphenyl)ethyl ethyl ether, n_D^{25} 1.4974 (reported (71) n_D^{20}

1.5080), infrared 1240, 1165, 1090, 1035, 825 cm.$^{-1}$, n.m.r. (CCl$_4$)

3.1(m), 5.77(q), 6.28(s), 6.79(q), 8.70(d) + 8.91$\mathcal{T}$(t), ratio

4.4:1:3:1.7:6 (calculated 4:1:3:2:6). Minor peaks were also present at

7.62, 8.08 and 8.50 $\mathcal{T}$ (total area ca. 2 per cent of peak at 6.28$\mathcal{T}$).

α-Phenylethyl bromide (37)

Anhydrous hydrogen bromide (23 g., 0.28 moles) was dissolved in

50 ml. of cold acetic acid, 20 g. (0.19 moles) of styrene added and the

solution left overnight at 0°. The mixture was then poured into water,

ether extracted and the ether extract washed with 10 per cent sodium

carbonate and water. The solution was dried over sodium carbonate and

fractionally distilled, yield 26 g. (73 per cent), b.p. 82-84° at 12 mm.,

n_D^{25} 1.5588 (reported (37) b.p. 85° at 13 mm., n_D^{25} 1.5612), equivalent

weight by Volhard titration 193 (calculated 185), n.m.r. (CCl$_4$) 2.7(m)

3.91(q), 8.01$\mathcal{T}$(d), ratio 5:1:3 (calculated 5:1:3). No styrene or

β-phenylethyl bromide was apparent in the n.m.r. spectrum.

α-(p-Methoxyphenyl)ethyl bromide

Hydrogen bromide was bubbled into a solution of α-(p-methoxy-

phenyl)ethanol (4.8 g., 0.032 moles) in 25 ml. of cold benzene for 5

minutes. The benzene solution was washed with water, 10 per cent

sodium carbonate and water again, dried over magnesium sulfate and the

benzene removed at reduced pressure, yield 4.7 g. Pentane was added,

the solution decanted from a viscous insoluble portion and the pentane removed at reduced pressure, n_D^{25} 1.5694, equivalent weight by Volhard titration 236 (calculated 215), n.m.r. 3.0(m), 4.89(q), 6.29(s), 8.03τ(d), ratio 6.2:1:4.5:3 (calculated 4:1:3:3).

α-Phenylethyl azide

α-Phenylethyl bromide (10 g., 0.054 moles) was added to a mixture of 20 g. (0.30 moles) of sodium azide, 40 ml. water and 160 ml. of acetone. The mixture was refluxed for two hours, poured into water, and ether extracted. The ether extract was washed with water, dried over magnesium sulfate and fractionally distilled, yield 4.4 g. (53 per cent), b.p. 106-107° at 41 mm., n_D^{25} 1.5242 (reported (39) b.p. 114° at 50 mm., n_D^{25} 1.5233), infrared (CCl$_4$) 2090, 1450, 1230, 695 cm.$^{-1}$, n.m.r. 2.77(s), 5.54(q), 8.58τ(d), ratio 5:1:3 (calculated 5:1:3).

Expected for $C_8H_9N_3$ C 65.28%   H 6.16%   N 28.55%

Found   C 65.24%   H 6.45%   N 28.35%
                           65.47%   6.19%   28.47%

α-(p-Methoxyphenyl)ethyl azide

α-(p-Methoxyphenyl)ethanol (10 g., 0.067 moles) and thionyl chloride (13.5 g., 0.11 moles) were allowed to react in 50 ml. of ether in a 125 ml. filter flask. The ether was removed at the aspirator, the residue dissolved in pentane and washed with water and 10 per cent sodium carbonate. The pentane was removed and the residue dissolved in 40 ml. of acetone. It was added to a mixture of 20 g. (0.31 moles) of sodium azide, 40 ml. of water and 120 ml. of acetone in a 500 ml. erlenmeyer. The mixture was stirred with a magnetic stirrer for one hour, poured into water and ether extracted. The ether extract was

washed with water, dried with magnesium sulfate and fractionally dis-

tilled, yield 4.6 g. (39 per cent), b.p. 139-140° at 23 mm., n_D^{25} 1.5319,

infrared (CCl$_4$) 2100, 1505, 1240, 1175, 1035 cm.$^{-1}$, n.m.r. 3.1(m),

5.60(q), 6.33(s), 8.60τ(d), ratio 4:1:3:3 (calculated 4:1:3:3).

Expected for C$_9$H$_{11}$N$_3$O   C 61.00%   H 6.26%   N 23.72%

Found   C 61.20%   H 6.44%   N 23.96%
                                  60.95%   6.26%

Stability of 2,6-dimethylbenzenesulfinic acid in 60% ethanol at 90° in the presence of sodium azide

2,6-Dimethylbenzenesulfinic acid (0.4744 g., 0.002733 moles) and sodium azide (1.1811 g., 0.01817 moles) were weighed out in a 100 ml. volumetric flask, 10 ml. Of 0.9747M 2,6-lutidine in 60 per cent ethanol added using an automatic pipette and made up to the mark with 60 per cent ethanol. The acid titre was measured by pipetting 5 ml. of the solution into 20 ml. of boiled distilled water. In some cases the aliquot was withdrawn from the flask at room temperature. In others the solution was heated at 90° in sealed tubes as indicated in Table XXXI.

Stability of α-phenylethyl azide and 2,6-dimethylbenzenesulfinic acid in 60% ethanol at 90° in the presence of sodium azide

2,6-Dimethylbenzenesulfinic acid (0.2920 g., 0.001682 moles), α-phenylethyl azide (0.2018 g., 0.001371 moles) and sodium azide (0.6570 g., 0.01011 moles) were weighed out in a 100 ml. volumetric flask, 10 ml. of 0.9747 M 2,6-lutidine in 60 per cent ethanol added using an automatic pipette and the solution made up to the mark with 60 per cent ethanol. The procedure was as described for kinetic runs with

α-phenylethyl 2,6-dimethylbenzenesulfinate with measurement of the
acid by titration and of the azide by the infrared method. The results
are reported in Table XXXII.

Resolution of α-phenylethanol (43)

A typical resolution is described.

α-Phenylethyl acid phthalate

A solution of 200 g. (1.64 moles) of α-phenylethanol and 250 g.
(1.69 moles) of phthalic anhydride in 1 litre of anhydrous pyridine in
a 2 litre round bottom flask was heated overnight on the steam bath,
cooled and poured on to excess ice-hydrochloric acid. The mixture was
ether extracted, the ether extract washed several times with water,
dried over magnesium sulfate and the ether removed at reduced pressure.
α-Phenylethyl acid phthalate crystallised from ethyl acetate-Skelly
Solve B, yield 295 g., m.p. 101-104°. It was recrystallised from the
same solvent mixture, yield 260 g. (59 per cent), m.p. 107-108° (reported
m.p. 108° (43)).

Brucine salts

Brucine (460 g., 1.17 moles) was added to a warm solution of
α-phenylethyl acid phthalate (315 g., 1.17 moles) in 1100 ml. of
acetone in a 3 litre erlenmeyer and left overnight. The mother liquors
were separated by decantation and the precipitated (-)-brucine salt
washed with a little acetone, yield 525 g.. This was recrystallised
from methyl acetate after removal of some insoluble material, yield
190 g. (25 per cent), m.p. 147-152° (reported m.p. 153°). "Practical
grade" methyl acetate is superior to "Reagent grade" for the

recrystallisation.

On scratching and standing for several days, the acetone mother liquors yielded 350 g., of (+)-salt which was recrystallised from acetone, yield 250 g. (32 per cent), m.p. 100-103° (reported m.p. 105°).

Active α-phenylethyl acid phthalates

The (+)-brucine salt (250 g., 0.38 moles) was treated with excess dilute hydrochloric acid in the presence of a little acetone. When reaction was complete the supernatent liquid was separated by decantation and ether extracted. The residual acid phthalate (the major portion of the product) was dissolved in ether, the combined ether solutions washed with water, dried over magnesium sulfate and the ether removed at reduced pressure. The yellow oil resulting was dissolved in 180 ml. of carbon disulfide and left overnight in an open 300 ml. erlenmeyer. The solution was then warmed and Skelly Solve B added. On cooling 58 g. (57 per cent) of (+)-α-phenylethyl acid phthalate was obtained, m.p. 78-82° (reported m.p. 86°).

The (-)-brucine salt (190 g., 0.29 moles) similarly yielded 52 g. (67 per cent) of (-)-α-phenylethyl acid phthalate $[\alpha]_D$ -60.4° (in CS_2, $\underline{l}$ = 1, $\underline{c}$ = 2.08) (reported $[\alpha]_D$ -65.8° in CS_2), optical purity 92 per cent. When (±)-acid phthalate separated from the CS_2 solution, as reported by Kenyon (43), the resolution gave α-phenylethanol of higher optical purity.

Active α-phenylethanol

(+)-α-Phenylethyl acid phthalate (58 g., 0.21 moles) was heated with 200 ml. (0.50 moles) of 10 per cent sodium hydroxide in a 500 ml.

round bottom flask and the α-phenylethanol formed by hydrolysis collected

by steam distillation. The distillate was extracted with ether, the

ether extract washed with water, dried over magnesium sulfate and the

solvent removed at reduced pressure, yield 24 g. (94 per cent), α_D +17.028°

(neat, $\underline{l}$ = 0.5), $[\alpha]_D$ + 34.0° ($\underline{l}$ = 1, $\underline{c}$ = 3.11) (reported α_D 11.04°

(neat, $\underline{l}$ = 0.25)), optical purity 77 per cent. The infrared and n.m.r.

spectra were superimposable on those of the racemic alcohol.

Similarly the (-)-phthalate (52 g., 0.19 moles) yielded 22 g.

(93 per cent) of (-)-α-phenylethanol, α_D -17.733° (neat, $\underline{l}$ = 0.5),

optical purity 80 per cent.

Active α-phenylethyl ethyl ether

This compound was prepared from the alcohol by Method A as

described for the racemic ether. (-)-α-Phenylethanol (α_D -19.552°,

optical purity 89 per cent) yielded (-)-α-phenylethyl ethyl ether,

α_D -35.072° (neat, $\underline{l}$ = 0.5), $[\alpha]_D$ -90.4° ($\underline{l}$ = 1, $\underline{c}$ = 3.10). Kenyon

(3) reports α_D -22.22° (neat, $\underline{l}$ = 0.25) for the optically pure com-

pound. Hence the above ether is 79 per cent optically pure and the

optically pure ether has $[\alpha]_D$ -115° (in EtOH, $\underline{l}$ = 1).

Active α-phenylethyl chloride

A solution of 15 g. (0.12 moles) of (-)-α-phenylethanol

(α_D -17.733°, neat, $\underline{l}$ = 0.5, optical purity 80 per cent) and 51 g.

(0.55 moles) of pyridine in 120 ml. of chloroform in a 500 ml. erlen-

meyer was cooled to -15°. Hydrogen chloride (10 g., 0.27 moles) was

then passed in and, without allowing the temperature to rise, 11 ml.

(19g., 0.12 moles) of phosphorus oxychloride was added. After standing

at room temperature for one day the solution was poured on to ice, the

chloroform layer washed with 85 per cent phosphoric acid, water and

10 per cent sodium carbonate and fractionally distilled, yield 9 g.

(55 per cent), b.p. 72-75° at 16 mm., α_D +41.802° (neat, $\underline{l}$ = 0.5°),

(reported (44) b.p. 68° at 8 mm.). The n.m.r. spectrum was super-

imposable on that of the racemic chloride.

Active α-phenylethyl 2,6-dimethylphenyl sulfide

(+)-α-Phenylethyl chloride (9 g., 0.064 moles, α_D +41.802°),

2,6-dimethylthiophenol (9 g., 0.065 moles) and sodium hydroxide (5 g.,

0.125 moles) in 150 ml. of 98 per cent ethanol in a 300 ml. round bottom

flask were refluxed for five hours. The mixture was poured into water,

ether extracted, the ether extract washed with water, dried over magne-

sium sulfate and the ether removed at reduced pressure, yield 14.5 g.

(93 per cent), $\left[\alpha\right]_D$ -182° ($\underline{l}$ = 1, $\underline{c}$ = 2.16), n.m.r. 2.96 + 3.09(2 sing-

lets), 6.10(q), 7.68(s), 8.48τ(d), ratio 8:1:6:3 (calculated 8:1:6:3).

Minor peaks were also present at 7.90, 8.63 and 8.74τ.

Active α-phenylethyl 2,6-dimethylphenyl sulfone

Oxidation of α-phenylethyl 2,6-dimethylphenyl sulfide with

hydrogen peroxide in acetic acid as described for the racemic compound

gave active α-phenylethyl 2,6-dimethylphenyl sulfone. Details of the

yield, rotations, etc., are given in Chapter II, page 84).

Tetrabutylammonium bromide

Butyl bromide (69 g., 0.50 moles) and tributylamine (93 g., 0.50

moles) were heated together in a 300 ml. round botton flask on the steam

bath for ten days. The product was stirred with ethyl acetate and the

crystalline salt collected by filtration. It was thrice recrystallised from ethyl acetate, yield 75 g. (46 per cent), m.p. 117.5-118.5° (reported (72) m.p. 119°).

Pyridine hydrobromide

Pyridine hydrobromide was prepared by bubbling hydrogen bromide into anhydrous pyridine. The precipitate was collected by filtration and washed well with ether.

Equilibration of diastereomers in pyridine in the presence of tetra-butylammonium bromide

Diastereomerically pure α-phenylethyl 2,6-dimethylbenzene-sulfinate (100 mg., 0.36 mmoles) and tetrabutylammonium bromide (90 mg., 0.28 mmoles) were dissolved in 0.6 ml. of pyridine and the solution sealed in a n.m.r. tube. The spectrum was taken and the tube placed in the 70° bath. It was withdrawn at intervals, cooled to room temperature and the spectrum taken.

Equilibration of diastereomers in pyridine in the presence of pyridine hydrobromide

A typical experiment is described. Diastereomerically pure α-(p-methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate (100 mg., 0.33 mmoles) and pyridine hydrobromide (9 mg., 0.06 mmoles) were dissolved in 0.7 ml. of pyridine and the n.m.r. spectrum taken. The solution was allowed to stand in a stoppered vial at room temperature and the spectrum taken at intervals.

Reaction of diastereomerically pure α-phenylethyl 2,6-dimethylbenzene-sulfinate in 60% ethanol at 90°

α-Phenylethyl 2,6-dimethylbenzenesulfinate (0.3430 g., 0.001250 moles) was weighed out in a 50 ml. volumetric flask, 5 ml. of 0.9696M 2,6-lutidine in 60 per cent ethanol added using an automatic pipette and the solution made up to the mark with 60 per cent ethanol. The solution was allowed to react at 90° in a 170 ml. pressure bottle for 21.5 hours (one half-life). It was cooled to room temperature, poured into water and ether extracted. The ether extract was washed with water (twice), 3N HCl and water (twice), dried over magnesium sulfate and the ether removed at reduced pressure. The n.m.r. spectrum was taken, the CS_2 solvent removed at reduced pressure. To ensure that no 2,6-lutidine remained the pentane solution was washed with 3N HCl and water, dried over mangesium sulfate and the pentane removed at reduced pressure. The n.m.r. spectrum was then redetermined.

Reaction of diastereomerically pure α-(p-methoxyphenyl)ethyl 2,6-dimethyl-benzenesulfinate in ethanol at 70°

α-(p-Methoxyphenyl)ethyl 2,6-dimethylbenzenesulfinate (0.2583 g., 0.0008453 moles) was weighed out in a 50 ml. volumetric flask, 5 ml. of 0.9649M 2,6-lutidine in ethanol added and the solution made up to the mark. The solution was placed in a pressure bottle in the 70° bath for 22 minutes (ca. one half-life), withdrawn and cooled to room temperature. The solution was poured into 100 ml. of ether and the ether layer washed with 100 ml. of water, 50 ml. of water, 50 ml. of 3N HCl, 50 ml. of water and 50 ml. of water. The ether solution was dried over potassium carbonate and the ether removed at reduced pressure.

TABLE XLVI

Hypothetical rate calculation for a mixture of diastereomers of α-phenyl-

ethyl 2,6-dimethylbenzenesulfinate

$$\left[A \right] = 2 \left[B \right], \; k_A = 1.4 \times 10^{-5} sec.^{-1}, \; k_B = 0.9 \times 10^{-5} sec.^{-1}$$

t(min.)	$OD_A(a)$	$OD_B(b)$	OD_{total}	log OD_{total}	$k \times 10^5 sec.^{-1}$
0	0.500	0.300	0.800	$\overline{1}$.9031	--
140	.445	.278	.723	.8591	1.20
310	.385	.254	.639	.8055	1.20
550	.315	.223	.538	.7308	1.20
985	.219	.176	.396	.5977	1.19
1600	.130	.126	.256	.4082	1.18
2120	.084	.095	.179	.2529	1.18

Mean = 1.19 $\pm$ .01

(a) Optical density due to isomer A.

(b) Optical density due to isomer B.

The same procedure was used in the run with added tetrabutylammonium

azide (kindly supplied by D. Darwish).

Sample hypothetical rate calculation

The results of a rate calculation for a 2:1 mixture of the fast

and slow diastereomers of α-phenylethyl 2,6-dimethylbenzenesulfinate

are reported in Table LXVI.

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